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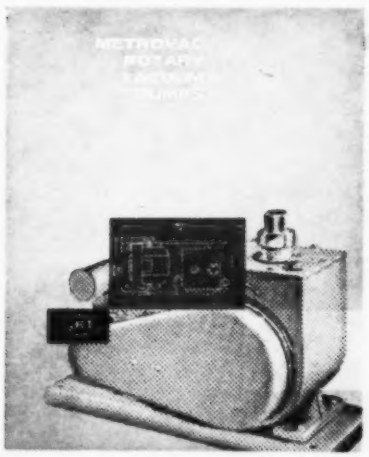

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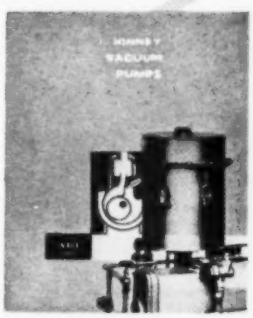

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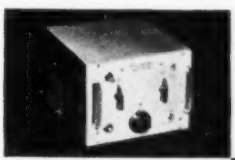

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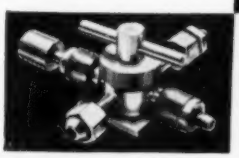

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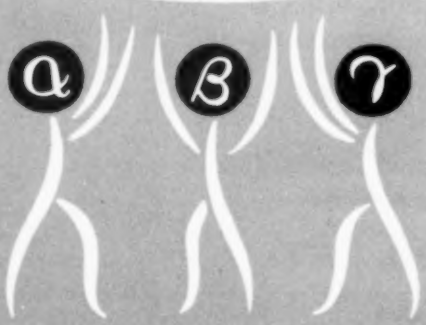

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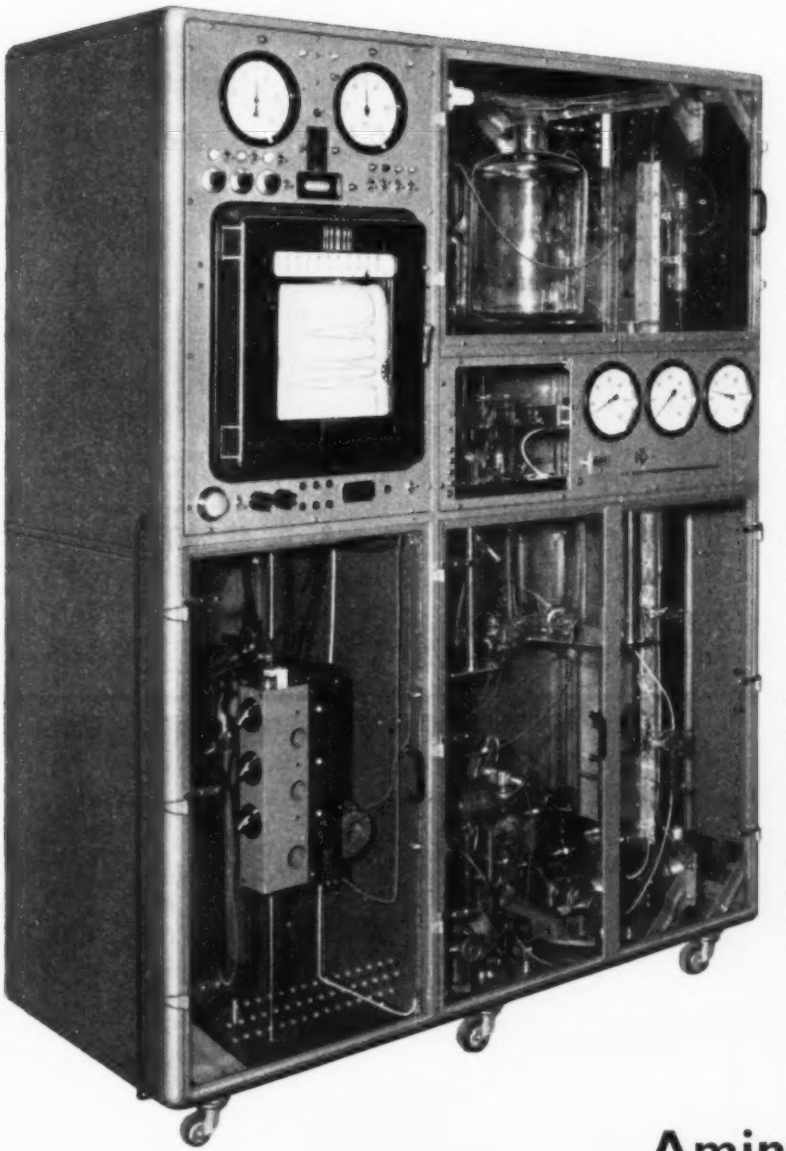

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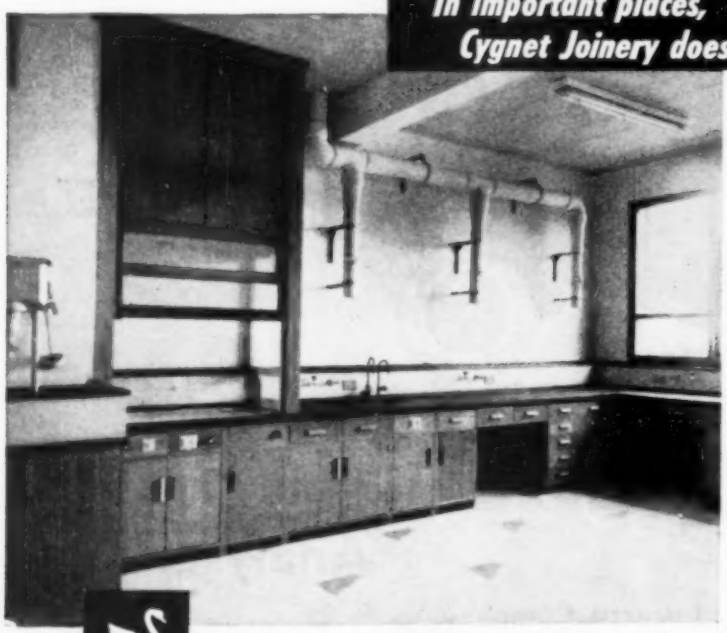

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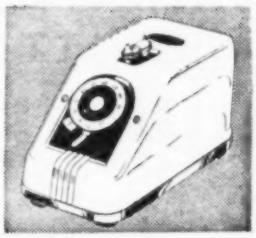

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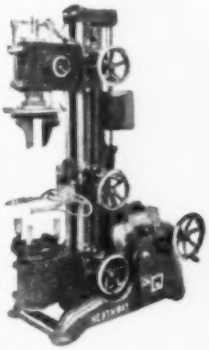

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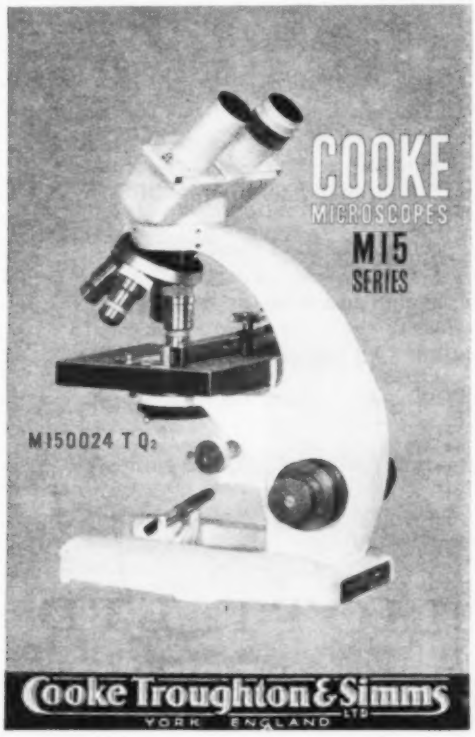

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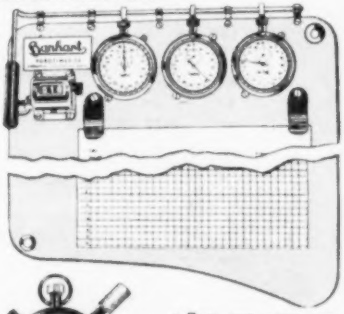

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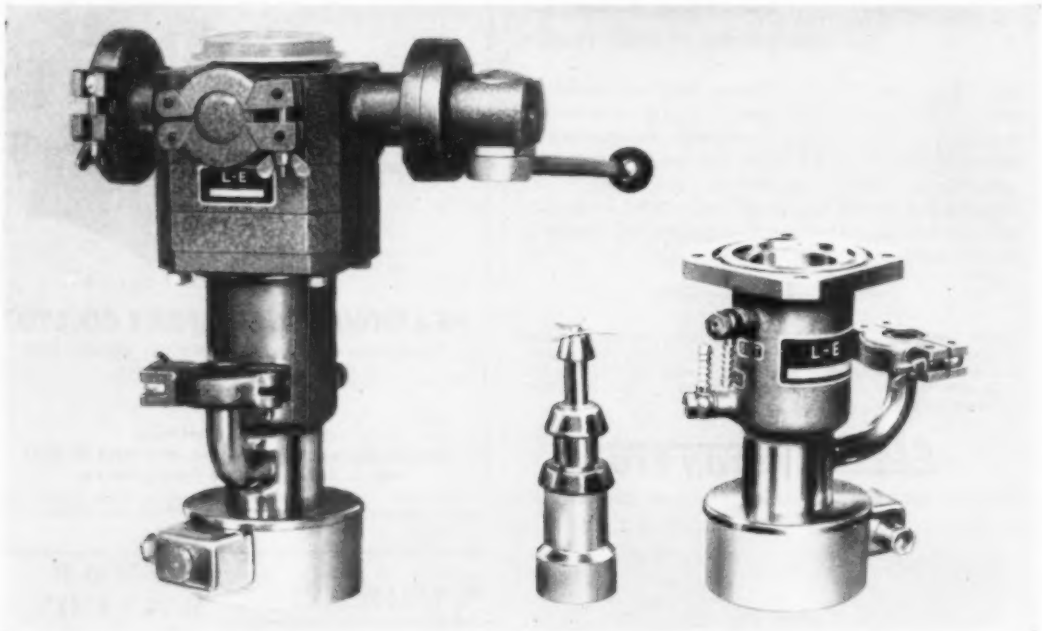

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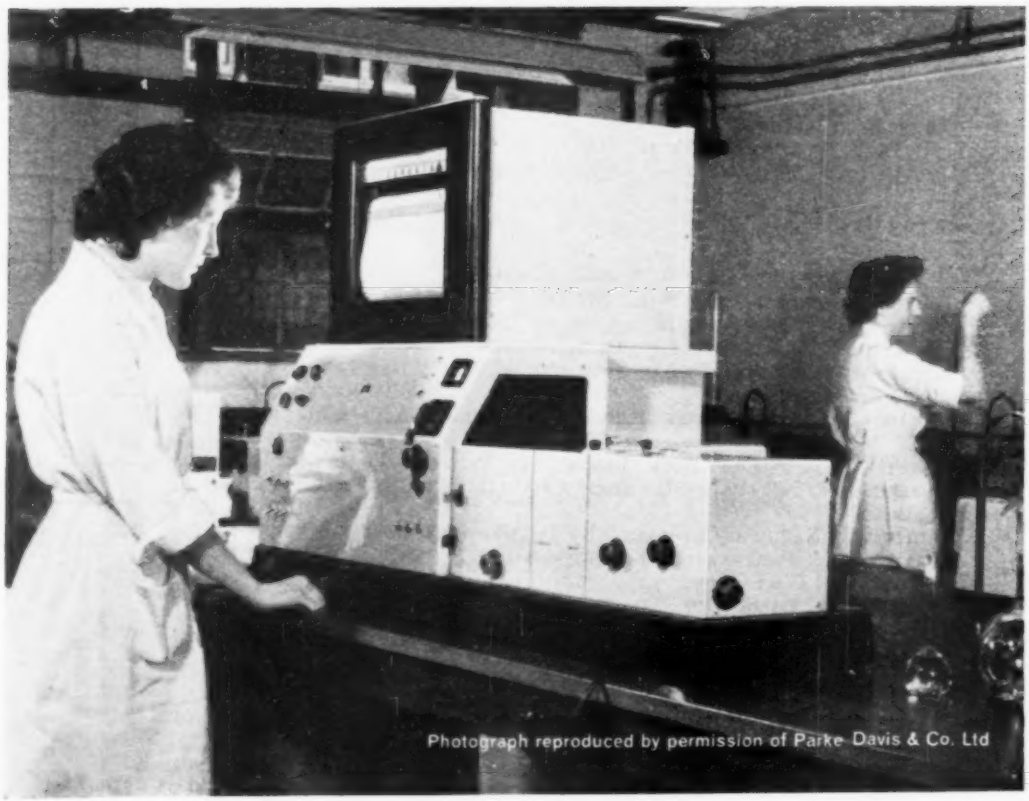

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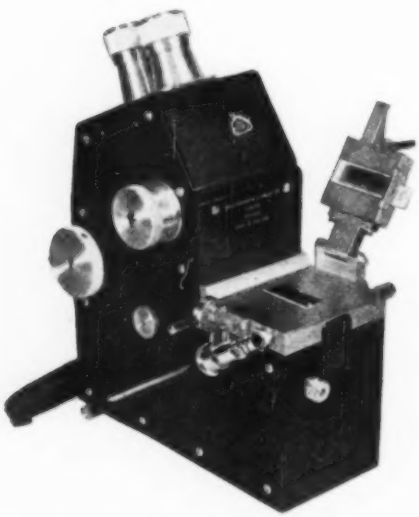

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RESEARCH AND DEVELOPMENT IN INDUSTRY

ALTHOUGH in the debate in the House of Commons on the nuclear power programme on February 3 the location of nuclear power plants in Britain was discussed, and some anxiety was expressed over the preservation of amenity, the serious criticism voiced in the latest report of the Nature Conservancy was not mentioned, and the debate dealt with many of the same issues as that on the economic situation which followed on February 6 and 7. These issues are also discussed in the PEP report, *Growth in the British Economy**, to which frequent reference was made in the latter debate. The debate on February 3, centred on a motion of Mr. J. Eden, which was accepted for the Government by Mr. J. C. George, Parliamentary Secretary to the Ministry of Power. The motion urged the Government, while giving due weight to considerations of public safety, the preservation of landscape, and the need to make power available from the cheapest and most efficient sources, to maintain the nuclear power programme at a level that would encourage the development of manufacturing experience and capacity, and provide the best possible prospects for exporting British designs, products and skill. Mr. Eden questioned the wisdom of development proceeding at the rate of about one new nuclear power station a year, and thought that serious waste of man-power and resources was involved in the maintenance of the industrial consortia and in competitive tendering, even by the three consortia now remaining out of five. He was also concerned that some of the stations now under construction might be obsolete fairly soon, and superseded by stations which could be built at lower capital cost and produce power more efficiently. He referred particularly to duplication of research and also asked for more positive encouragement in connexion with exports.

Some of these points were also emphasized by Mr. N. Ridley and by Mr. A. Neave. Mr. Neave referred to the bearing of the load factor, and said that with a load factor of 75 per cent, the cost of nuclear generation might soon approximate to 0·5*d*. per unit. He also urged that the Atomic Energy Authority should make full use of the industrial consortia in the design and development of reactor systems and suggested that, in particular, the Authority should be encouraged to look into new systems, and the advanced conversion of existing reactor systems. He stressed the need for the industry and its technologists to be able to plan ahead with some confidence that the programme would not again be curtailed, but was obviously doubtful whether it is economic to maintain the three industrial consortia, employing altogether some 1,000 scientists and engineers, to produce one station for every three years per consortium. Mr. R. Gunter was also concerned about the effective and economic use of the limited trained man-power in Britain; but Mr. D. Price challenged the view that there is duplication of research and development and thought we should keep at least two of the consortia. It is not easy, he pointed out, to build up again a team that has once been disbanded, and he strongly supported the view that the consortia should be encouraged to participate in development. He thought the area of advance in research on reactor design should be broadened and that, besides associating the consortia more closely with the Atomic Energy Authority, we should make more use of the European Nuclear Energy Agency. Mr. T. H. H. Skeet was concerned more particularly with the design of reactors for export, pointing out that the nuclear power plant of 300–500 MW. produced for the United Kingdom may be too large for some overseas markets.

In replying on the debate, Mr. J. C. George stated that the commissioning of the experimental fast reactor at Dounreay is proceeding satisfactorily; but in regard to controlled thermonuclear reactors, the Authority has broadened its programme of research with a number of experiments aimed at developing the advanced techniques required. He claimed that the present programme, with six nuclear power stations under construction, two more to be started in the next twelve months, and permission sought for another, is sufficient to sustain an industry capable of competing with success abroad and expanding to meet our own needs. He quoted figures for falling costs, from £160 per kW. at Berkeley to £123 at Trawsfynydd and £110 at Dungeness, and said that, besides two stations already sold abroad, there are possibilities of two in India, one in Brazil and one in Japan, apart from the export of research reactors. As regards small reactors, the first might well be on merchant ships, but it does not seem possible, he said, to construct a small nuclear station to provide power at anything like an economic price.

This debate showed that the House of Commons is fully alive to the importance of research and development as a basis in economic growth, and to the need for care to avoid waste of trained man-power. These factors also received some emphasis, though to a lesser extent, when the economic situation generally was debated. Mr. R. E. Prentice, who directed attention first to the wastage of skills, was primarily concerned with this in respect of the re-training of skilled men who had lost their existing jobs, and with apprenticeship; but although he and other speakers referred to the lack of support for the Government's scheme of training young people, no reference was made to the waste caused through the inappropriateness of apprenticeship schemes and the

* *Growth in the British Economy: a Study of Economic Problems and Policies in Contemporary Britain.* Pp. xii+256. (London: Political and Economic Planning; and George Allen and Unwin, Ltd., 1960.) 30*s*. net.

maintenance of periods of apprenticeship which are quite unnecessary under modern conditions. On this point generally, Mr. C. Fletcher-Cooke was forthright, condemning the hoarding of skilled labour, and urging that the skilled labour force should be expanded by putting through group apprenticeship and other means of industrial training with real urgency. He also advocated an intensive study of the whole question of the psychology of the mobility of labour.

So far as research and development are concerned, the comments made in the debate related rather to the insufficiency of research in two particular industries, namely, the shipbuilding and machine tool industries, though Mr. S. R. McMaster stressed the need for adequate expenditure on research and development generally as a factor in encouraging higher productivity, and referred to the need to afford adequate support for university research. Both these industries have been the subject of recent inquiry. The machine tool industry was sharply criticized by the Mitchell Committee for its lack of expenditure on research and development, which appears to be a primary reason why imports of machine tools into Britain remain at a high level, and Britain's share of the trade of major importing countries, excluding eastern Europe and China, is less than half Western Germany's and no greater than that of Switzerland. Further, only 1·3 per cent of the employees in the machine tool industry are qualified scientists, compared with figures of 2·2 per cent in electrical engineering, 3·7 per cent in chemical industry and 2·7 per cent in the aircraft industry, and only 0·29 per cent of its technical men are employed on research.

In this comparison, the shipbuilding industry shows up even worse. Only 588 qualified scientists and engineers were employed in the shipbuilding and ship repairing industry at the beginning of 1959—about 0·6 per cent of the number of employees—and Mr. Austen Albu, in a recent broadcast talk on the price of tradition in industry, questioned whether more than 70 or 80 graduates are employed in the shipbuilding and marine engineering industry, and of these more than half are probably employed on Admiralty research. The report from the Department of Scientific and Industrial Research entitled *Research and Development Requirements of the Shipbuilding and Marine Engineering Industries**, which was freely mentioned in the debate, was highly critical of the industry; but the published material has been the subject of some criticism as representing only a part of the report. It was published however, with the concurrence of the Shipbuilding Conference, as representing the shipbuilding and marine engineering industries, and its recommendations have been agreed between that Conference, the Ministry of Transport and the Department of Scientific and Industrial Research. That should assure the implementation of its recommendations; but it is disturbing to find that objections have been raised by the boiler-makers to the comparisons of efficiency in the United Kingdom and elsewhere, and particularly the analysis of labour costs.

Neither here nor elsewhere are closed minds likely to encourage growth in the British economy, and the conclusions of the report are disturbing enough in their brevity. The world shipbuilding industry is itself facing a major and probably prolonged recession, and there is no indication that the United Kingdom industry has on balance any marked technical or economic advantage over its major foreign competitors, apart from its large home market. The total effort at present devoted to research and development in the field of shipbuilding and marine propulsion is insufficient in relation to the serious problems now facing the industry; in particular, practically no organized research has yet been applied to production and management problems with the object of increasing the productivity of labour and capital and reducing costs. While adequate effort is probably being devoted to problems of hull resistance and propeller design, the development of propulsion installations is handicapped by the organizational structure of the industries producing propulsion units and auxiliaries and, in consequence, by the insufficient use of available research facilities.

The figures quoted in this report for the research effort do not quite agree with those given by Mr. Albu. Of the total professionally qualified staff of 1,240, 247 are estimated to be employed on research and development, and the total expenditure on research and development in the industry is estimated at about £1·5 million, or 1·0 per cent of net output. When the contributions made to co-operative research in the British Shipbuilding Research Association, the Parsons and Marine Engineering Turbine Research and Development Association and the British Welding Research Association and to the Ship Division at the National Physical Laboratory are added with the Government contributions, total annual expenditure on research in and for the industry is probably about £2·5 million, or 1·7 per cent of net output; in marine engineering alone, however, it is about £1·9 million, or about 4·4 per cent of net output, a figure which compares favourably with most other manufacturing industries. Nevertheless, there is some evidence tending to confirm that British shipbuilding costs have recently been high by comparison with those of major competitors, and there is no evidence to suggest that over the industry as a whole labour productivity has significantly increased, in spite of increased investment in production plant and machinery. Average construction times in 1957–59 were at least double those in Germany, Sweden and Japan, and it seems certain that the fullest use of shipyard space and capital equipment is handicapped by labour conditions and by the impracticability of shift working.

The report recommends that the Department of Scientific and Industrial Research and the Shipbuilding Conference, in collaboration with the Ministry of Transport, should take further steps to examine the research and development needs of the industry

* Department of Scientific and Industrial Research. *Research and Development Requirements of the Shipbuilding and Marine Engineering Industries*. Pp. vi+18. (London: H.M. Stationery Office, 1960). 1*s*. 6*d*. net.

as a whole, and to review the facilities for carrying out research. Arrangements should be made for a concurrent economic and technical study of these needs in marine engineering to provide background for consideration by the Council for Scientific and Industrial Research of the reports it is to receive from the two research associations on their organization and programmes, and this study should be carried out by the Department of Scientific and Industrial Research with the assistance of the Ministry of Transport. The Department and Ministry should also consider with the industry what assistance can most appropriately be given to the industry's own efforts to promote research into production techniques and methods aimed at increasing productivity and reducing costs. As an immediate stimulus to development, the Department of Scientific and Industrial Research should give priority consideration to proposals for development under contract in these industries and with the Ministry of Transport, and the shipping industry should consider what further steps should be taken to study the industry's future technical requirements.

The President of the Board of Trade, Mr. R. Maudling, in concluding the debate on the economic situation, agreed that research and development generally need expansion. He also expressed the hope that the Mitchell Report on the machine-tool industry would point the way to a considerable expansion of research and development facilities in that industry—the report recommended that the industry's expenditure on research should be trebled. Expansion there and in the shipbuilding industry, however, as well as in nuclear power, needs to be considered in relation to the country's research and development effort generally and to the available resources in scientific and technical man-power. It is clear that the broad question is one to be considered further by the Minister for Science and his Advisory Council for Scientific Policy, for it is in this context that proposals for space research are properly considered, and also the steps to be taken to meet other shortcomings in the research effort of Britain to which the survey carried out for the Advisory Council and outlined in its last annual report pointed.

COLOUR VISION

Mechanisms of Colour Discrimination

Proceedings of an International Symposium on the Fundamental Mechanisms of the Chromatic Discrimination in Animals and Man, held in Paris, 25–29 July, 1958. Edited by Yves Galifret. (Sponsored by the International Council of Scientific Unions.) Pp. viii + 296. (London and New York: Pergamon Press, 1960.) 63*s*. net.

THIS book is a report of a very interesting conference at which ten invited papers were given. These introduced a series of valuable discussions which are fully reported. About seventy per cent of the report is in English, twenty per cent in French and ten per cent in German. The topics discussed fall under the following headings: (1) zoological inventory (including a paper on colour vision in insects by Von Frisch); (2) neurophysiological problems (including papers by Rushton on retinal processes and by Galifret on the optic nerve pathways); (3) visual pigments of colour vision; (4) psychophysical problems.

Perhaps the most interesting single issue was the relation between the trichromatic theory (Young, Helmholtz) and the opponent-colour theory (Hering). The exposition of the trichromatic theory (and of its limitations) by Stiles formed an admirably clear statement. Hurvitch gave an interesting exposition of the opponent-colour theory. It was unfortunate that his paper was entitled "The Tetrachromatic Scheme", thereby suggesting that the opponent-colour theory is an alternative to the trichromatic theory. The same information may be analysed (i) in terms of three primaries, or (ii) in terms of (*a*) total luminance (which may be called the white-black difference), (*b*) the red-green difference and (*c*) the yellow-blue difference. The psychophysical data and the electrophysiological observations of De Valois show that both these analyses are 'represented' in the visual cortex. Many other experiments, including the recent work of Svaetchin and MacNicol and of Wagner and Wohlbarst, indicate that signals relevant to both analyses are present at lower levels. It is very probable that eventually the trichromatic and opponent-colour concepts will be seen as aspects of one theory, as has happened with the wave-particle 'conflict' in physics.

Dartnall, who gave a very interesting paper on the biochemistry of cone pigments, opened with the statement that "no-one can say *with certainty* that he has ever had a cone pigment in a test-tube", and although this statement may be a little too cautious, the biochemical side of colour vision is certainly very difficult. Rushton, using biophysical methods, has been able to obtain the absorption spectra of two cone pigments and to show that one is absent in protanopes, but this does not identify the molecular structures.

This is not a book for the general reader, but I recommend it most strongly to all who are working in any part of this field. I would like to record my gratitude to M. Pieron who, as chairman, led the discussions and drew out so many ideas of value, and to M. Galifret both for his own paper and for editing this volume.

R. W. DITCHBURN

RAINFALL IN BRITAIN, 1957

British Rainfall, 1957

Report on the Distribution of Rain in Space and Time over Great Britain and Northern Ireland during the Year 1957 as recorded by about 5,000 Observers. (Ninety-seventh Annual Volume). Air Ministry: Meteorological Office. Pp. iv + 245. (M.O. 663.) (London: H.M. Stationery Office, 1960.) 32*s*. 6*d*. net.

THE volume of *British Rainfall* under review is the ninety-seventh of the series and covers the year 1957. It contains the usual tables, charts, and descriptions of the annual, seasonal and monthly amounts of rainfall and numbers of days with rain over Great Britain and Northern Ireland based on

observations at 5,022 stations. There are also the usual tables of heavy rainfalls with descriptions of the weather situations in which they occurred.

The general pattern was a decidedly wet first quarter, a very dry second quarter, a wet third quarter and a dry last quarter. The year as a whole had an average rainfall over England but a few per cent more than average over Scotland, Northern Ireland and Wales. Evaporation, too, was about average on the whole with a large value for June, the sunniest since 1909. The largest falls of rain in one day were 6–8 in. over the Camelford area of Cornwall in thunderstorms on June 8.

A new feature in this volume is a snow survey which is for the winter 1956–57 and gives a description of snowfalls and a table of the number of days of snow lying in the mountainous areas.

G. Stanhill, of the National Vegetable Research Station, contributes an article on the variance and co-variance of evaporation and rainfall for seven well-distributed stations, which brings out the importance of taking the variance of evaporation into account in computing the variance of the water content of the soil.

An important change in the main table of stations is the omission of the particulars of the type of gauge to make room for the National Grid reference locating the position of the gauge to the nearest 100 metres. This is a reflexion on one hand of the necessity for accurate knowledge of position in connexion with the more detailed studies of areal distribution of rainfall now required, and on the other hand of the great progress towards standardization of equipment and exposure produced by the much-intensified programme of inspection of gauges by the Meteorological Office.

The preface shows that consideration is being given to the need for continuing the use of such terms as 'rain-day', 'drought', etc., specified arbitrarily in terms of the rainfall amount of one day or a period in view of the possibility of readily obtaining frequency distributions of amounts or spells by the new machine methods of data-processing now coming into use. Comments on this point are particularly invited by the Meteorological Office.

No review of *British Rainfall 1957* would be complete without a mention of the fact that 1957 was the last year of official service of Dr. J. Glasspoole, who joined the British Rainfall Organization in 1916 and was associated with its work for more than forty years.

EXPLORING THE OCEANS

Frontiers of the Sea

The Story of Oceanographic Exploration. By Robert C. Cowen. Pp. 307+21 plates. (London: Victor Gollancz, Ltd., 1960.) 25*s.* net.

IN an expanding branch of science there is a clear need for the good 'popular' book, which can present achievements and aims not only to the general reader but also to scientists in other fields, and may even enable the specialist to see his own work in a truer perspective. Oceanography has been well served by such books in recent years, and that of Robert Cowen is a worthy addition to their number. The author sets out to cover the whole field of marine science, putting present knowledge in its historical setting and indicating the probable lines of future advance. He has achieved success in this comprehensive aim by a balanced selection of topics, which he has treated clearly and vividly.

After a historical introduction, the author discusses present ideas on the origin of the Earth and the oceans. He then describes some of the remarkable new features of bottom relief discovered by recent expeditions. An account is given of the use of oxygen isotope and radiocarbon techniques in the study of sediments and of geophysical methods for probing deeper into the ocean floor. In a chapter on ocean currents, the Gulf Stream is selected as an illustration of the complex structure revealed by modern techniques, and the sub-surface Cromwell Current as one of the major discoveries of recent years. The study of life in the oceans is represented by a chapter on plankton and a brief review of the larger forms of life, giving special attention to deep-living animals.

Having surveyed the present scene, the author looks to the future and to the possibility of exploiting the resources of the oceans, as a source of food and of minerals. In a final chapter on "The New Oceanography", he describes the bathyscaphe, the mesoscaphe and the abyssal submarine, the *Aluminaut*, now being developed. The 'Mohole' project and the problems of the disposal of radioactive wastes at sea are also discussed.

In a book with so many excellent features one is reluctant to look for faults. Some of the line drawings, however, are far from precise, and it would be almost impossible for anyone unfamiliar with the instruments concerned to understand the working of, for example, the water bottles in Fig. 4 or the Kullenberg corer in Fig. 12. There are several factual errors, a serious one being the statement, on p. 201, implying that the nutrient substances account for 6 per cent of the salinity of the sea, an estimate which is too great by several orders of magnitude.

K. F. Bowden

HISTORICAL GEOLOGY

Géologie Stratigraphique

Par Prof. Maurice Gignoux. Cinquième édition complétée d'un addendum par Léon Moret. Pp. iv + 760. (Paris: Masson et Cie., 1960.) 71 NF

THE data of stratigraphy are in themselves as dry as the dust of the Permian deserts. Undergraduate students of geology often look on stratigraphy as mere meaningless lists of names of formations and of fossils which occur in them. And of course the details of stratigraphy are meaningless unless they are related to specific problems. That is why *Principles of Stratigraphy* by C. O. Dunbar and J. Rodgers has such appeal; it concerns itself with problems of facies interpretation, and the relevance of all the detail is obvious to the reader. Similarly, L. J. Wills's *Physiographical Evolution of Britain* was such a success because the detail was related to problems of diastrophism. Much of the data of stratigraphy is, however, only relevant to problems of the subdivision and correlation of successions, which are problems not in themselves interesting though they may be important in the

working out of tectonic structures. It is obviously pointless that the student should burden his memory with excessive detail of this kind. Nevertheless, a certain modicum of general knowledge of successions every student must have; and he does need a text-book to which he can turn for such information when he has to orientate himself in the local setting of a particular problem. Ever since 1926, M. Gignoux's *Géologie Stratigraphique* has been available for this purpose.

It is in many ways a first-class text-book which covers the general stratigraphy of Western Europe very fully and provides also useful information about broad features of the stratigraphy of the rest of the world. Its outstanding characteristic is clarity and simplicity. It can and should be read in French by every student of geology with the least knowledge of the language. It is true that a translation of the fourth edition (1950) is now available. (This fifth edition, published since the death of the author, differs only in having an appendix giving references to a great many recent papers.) But reading this book in French leads the undergraduate student so naturally and painlessly to a knowledge of the French technical terms he will need in reading original papers that it is well worth his trouble.

In its successive editions the book has been considerably extended and continuously brought up to date. Numerous references to original papers cited in footnotes have been added in each edition. In many respects, however, the book does have an old-fashioned look—names like *Glyphioceras*, *Anthraconauta* and *Posidonomya* have not been emended, the Palaeocene is not recognized, and the Calabrian (Villafranchian) remains in the Pliocene.

The great feature of this book is its treatment of the Mesozoic and Cainozoic of France and North Africa. There is no better introduction to the complicated stratigraphy of the Alps than can be had from the splendidly lucid sections of successive chapters devoted to this subject. The new appendix to this edition by Prof. L. Moret contains a special section with numerous references to recent literature on the French Alps, with his own critical comments. This is a particularly valuable addition to that part of the book which is of most interest to the non-French reader.

S. Simpson

THE JESSE P. GREENSTEIN MEMORIAL SYMPOSIUM

Amino Acids, Proteins and Cancer Biochemistry

Papers presented at the Jesse P. Greenstein Memorial Symposium, Division of Biological Chemistry, American Chemical Society, September 16, 1959. Edited by John T. Edsall. Pp. ix+244. (New York: Academic Press, Inc.; London: Academic Press, Inc. (London), Ltd., 1960.) 7 dollars.

JESSE GREENSTEIN died in 1959 and his scientific publications cover the three decades, 1930–60. All his work carried a sense of building, stone on stone—a painstaking insistence on the surest foundations so that the final result should be as sound as man could make it. He was a pioneer in amino-acid, peptide and protein chemistry all his life and, for many years, was also actively pursuing a vast programme of work on the enzymology of cancer tissues. This dual thread of endeavour running through his life's work was reflected in the contributions to the symposium held in his memory, lending them a coherence which makes their record in this volume a most gratifying one to read.

The first part contains a study by Winitz and other colleagues at the National Cancer Institute extending the series of nutritional experiments using water-soluble, chemically defined diets, which they began with Greenstein in 1957. There are papers on the structure of ribonuclease (Scheraga *et al.*) and of carboxypeptidase *A* (Neurath *et al.*); on the chromatographic evaluation of protein mixtures (Sober and Peterson), and a stimulating contribution by Alton Meister on the activation of amino-acids and the biosynthesis of peptide bonds.

The second part of the symposium stems from Greenstein's interest in cancer research. Weinhouse enlarges on Greenstein's concept of the biochemical uniformity of tumours: that different tumour tissues resemble one another in their biochemical characteristics more closely than they do their tissues of origin. He relates this generalization to a critical consideration of the 'deletion' hypothesis of the cause of cancer and comments on Greenstein's evidence for multiple enzyme deletion in neoplasms, concluding, pertinently, that since so many enzymes appear to suffer deletion after a cell becomes malignant, evidence of far greater cogency will be required before cancer initiation can be ascribed to any specific change of this type.

Roberts and Simonsen, and Saul Kit contribute chapters respectively on the free amino-acids and on the nucleic acids of normal tissues and tumours, and the symposium ends with a fine flurry of fact and speculation over which Racker and Britton Chance preside with easy control. Much of their argument is concerned with the search for a rate-limiting factor in the carbohydrate metabolism of cells, with special reference to the ascites tumour cell. The significance of adenosine diphosphate and of inorganic phosphate in this connexion is expounded and stress laid on the 'compartmentation' of adenosine diphosphate—and of reduced diphosphopyridine nucleotide—into cytoplasmic and mitochondrial forms. A comparable distinction of inorganic phosphate into endogenously formed P_i and slowly diffusible extracellular P_i, underlines the importance of knowing 'readily available' substrate and coenzyme concentrations when considering rate-limiting conditions in the cell. Explanations of both the Pasteur effect and of the well-known phenomenon of lactate production in the respiration of tumours are tentatively given with the aid of the hypotheses outlined. Britton Chance, it must be added, pursues the subject to the point of digital computer representation.

Certain interesting differences come to light in these two chapters, including a basic one on the estimation of hexokinase activities, and another on the effect of glucose on respiring ascites tumour cells (pp. 178 and 199). They may be taken as typifying the general liveliness of the text throughout the book.

"No-one can measure the full impact of the contributions of an outstanding scientist", writes Dr. Edsall in his preface; but those colleagues of Dr. Greenstein who have written in this symposium have finely acknowledged their debt and friendship.

F. H. Malpress

Beyond the Planet Earth

By Konstantin Tsiolkovsky. Translated from the Russian by Kenneth Syers. Pp. vi+190. (London and New York: Pergamon Press, 1960.) 15s. net.

WRITTEN in 1920, this mildly prophetic tale is described as a 'scientific fantasy'. It is well above the ordinary run of science fiction, in that the characters behave as normal human beings for most of the time, the laws of physics are also undistorted, and the author was clearly a competent scientist. As to prophecy, the longest shot occasionally finds its mark, and any consistency between fantasy and later fact need not affect its attractiveness as a fable. The preface has a lot to say about Tsiolkovsky's work on rockets, which seems to have been done unobtrusively and unsubsidized, but led to his being named as the "father of the *Sputniks*"; and some other aeronautical priorities seem to have slipped in under this umbrella. The book itself was intended to be entertaining, and is a good story.

The characters are a lively bunch; Franklin, Galileo, Helmholtz, Laplace, Newton, and the inventive Ivanov. They start operations in lush headquarters remote from modern life, which has by 2017, when they start up, become depressing. The base is a castle in the Himalayas (it will be remembered that Jules Verne had already annexed the Carpathians). They work things out, get into orbit, live graciously without gravity, find gold and precious stones on the Moon, and, after some years of resourceful exploration, land happily in the Indian Ocean to start the 'space era' going. The chief re-entry problems are the dreadful colds and influenza to which they succumb on returning to the rigours of ordinary life. A simple and almost unsophisticated story, it has been very readably translated; Mr. Syers has the Arthur Ransome touch.

G. R. NOAKES

Technology, Engineering and Safety

Vol. 2. Edited by R. Hurst, R. N. Lyon and C. M. Nicholls. (Progress in Nuclear Energy, Series IV.) Pp. xvi+799+xii. (London and New York: Pergamon Press, 1960.) 105s. net: 15 dollars.

THE present volume is the fourth in a series of eleven, and consists of a selection of thirty-four papers presented at the 1958 Geneva Conference on the peaceful uses of atomic energy, together with a short introduction by C. M. Nicholls. The papers are presented under the following chapter headings: Reactor Chemistry; Reactor Materials; Engineering Experience and Practice; Engineering Studies; and Engineering Aspects of Reactor Safety. The editors have recognized the difficulty of making a representative selection from the large number of relevant papers, and acknowledge that in some cases the choice has been somewhat arbitrary. The book covers a very wide field and includes a number of papers on various aspects of advanced reactors, such as the liquid metal fuelled reactor and molten fluoride systems which do not, however, figure prominently in present-day reactor development programmes. Nevertheless, the information presented forms a useful and interesting record of the considerable research and development work undertaken in support of these ambitious concepts. The eight papers on various aspects of reactor safety form an interesting group, and those dealing with the containment problem constitute a useful introduction to a difficult subject about which there is still a considerable diversity of opinion.

The volume represents a convenient—if somewhat expensive—summary of various aspects of reactor technology and safety, especially for those who do not have ready access to all the Geneva Conference papers. As such, it forms a useful addition to the present series.

D. ENGLISH

High-Energy Electron Scattering Tables

By Robert Herman and Prof. Robert Hofstadter. Pp. ix+278. (Stanford, Calif.: Stanford University Press; London: Oxford University Press, 1960.) 68s. net.

THIS volume of tables is designed to serve as a handbook for those concerned with high-energy electron scattering. It contains numerical values of nuclear charge density distributions, form factors of nucleons and light nuclei and cross-sections for electron-electron scattering. There is also a number of excellent figures showing point proton cross-sections and other data. The tables are preceded by a review of the theoretical basis of the calculations which may well be of wider interest, as it includes a discussion of Born approximation calculations and their accuracy, the choice of models for nuclear density distributions, and also a more detailed treatment of electron scattering by nucleons and deuterons.

A large part of the work on these topics has been carried out at Stanford University by Prof. Hofstadter and his associates. This book gives further indication of the power of the electron scattering techniques they have developed for the investigation of nuclear structure and sizes.

D. F. JACKSON

The Year Book of the Royal Society of London, 1961

(No. 65.) Pp. 302. (London: The Royal Society, 1961.) 21s.

THE *Record of the Royal Society of London* for 1897 outlines in its preface the purpose of the then newly inaugurated *Year Book* as "containing information which is liable to change". The *Year Book* of the Royal Society is a most valuable compendium for anyone who wishes to keep track of many leading scientists. Much information can be gleaned from its 302 pages, concerning Fellows and Foreign Members, membership of the many committees and boards, standing orders, Council procedure, medal awards, lectures, financial trusts and funds, special memberships and appointments, and a report of Council for the year ended September 30, 1960—a year in which the Society celebrated the tercentenary of its foundation. Appended to the report of Council are twenty-five reports on research work carried out by individuals holding Royal Society research fellowships. Without doubt, the lists of Fellows and Foreign Members is one of the most useful sections of the *Year Book*. However, anyone who is constantly having to refer to this part of the *Year Book* will be well aware that the information available is only valid to January 1, and that continual reference is necessary to the supplementary 'fly-sheet', when it becomes available. As has been advocated in these pages in previous years, it is to be regretted that publication of the *Year Book* is not withheld until May, by which time it should be possible to include the new Fellows elected in the current year.

INTERSTELLAR AND INTERPLANETARY COMMUNICATION BY OPTICAL MASERS

By Dr. R. N. SCHWARTZ and Prof. C. H. TOWNES*

Institute for Defense Analyses, Washington, D.C.

LONG-RANGE communication by radio-waves is already well known, and the possibility of interstellar communication by radio-waves in the microwave region has been suggested in several interesting proposals[1-3] to search for signals from intelligent beings on planets associated with nearby stars. The supposition is that curiosity such as our own would motivate advanced civilizations associated with stars other than our Sun to make determined efforts to communicate with whatever other intelligent life might exist on neighbouring planetary systems. Radio-waves have, because of our present state of technological development, dominated the field of very long-distance communication, and perhaps for this reason these proposals gave particular attention only to the radio region. It appears, however, that we are now not very far from the development of maser oscillators and other appropriate apparatus in or near the optical region which will also allow detectable light signals to be beamed between planets of two stars separated by a number of light years.

Our own maser techniques in the optical and nearby spectral regions are still in a rudimentary stage; no such operating device was known a year ago[4,5]. Another ten years should bring very marked development. Further, only historical accident seems to have prevented discovery of optical masers thirty or more years ago, in which case they would probably already have been in an advanced stage of development. This implies that a separate civilization might have inverted our own history and become very sophisticated in the use of optical or infra-red masers rather than in the techniques of short radio-waves.

We propose to examine the possibility of broadcasting an optical beam from a planet associated with a star some few or some tens of light-years away at sufficient power-levels to establish communications with the Earth. There is some chance that such broadcasts from another society approximately as advanced as we are could be adequately detected by present telescopes and spectrographs, and appropriate techniques now available for detection will be discussed. Communication between planets within our own stellar system by beams from optical masers appears *a fortiori* quite practical.

Optical Maser Characteristics

Present ruby masers have produced pulsed optical beams of 10-kW. power[6], or still shorter pulses of perhaps 100-kW. peak power. This radiation is concentrated in a band-width of about 0·02 cm.$^{-1}$. Another type of maser, operating continuously at about 0·02 W., emits a wave which has been shown to be in phase over the entire maser reflector surface (about $\frac{1}{2}$ in. in diameter) and to be concentrated in a frequency-interval of about 10 kilocycles per sec.[7]. The latter case is much closer to theoretical expectations[8] for an ideal maser in so far as coherence is concerned. There seems to be no general reason, other than the necessary dissipation of power, why solid-state optical masers cannot operate continuously at high power and with a short-term monochromaticity close to theoretical expectations, or hence with frequency-widths very much less than 1 megacycle/sec.

Now consider directivity of the beam from an optical maser. If a maser produces a wave of wavelength λ with constant phase over a surface of diameter d, the angular width of the radiating beam is approximately λ/d. However, it is obvious that its angular width can be still further reduced if it is operated in conjunction with an auxiliary optical system. Imagine that an ideal lens is put in the beam of focal length d and diameter d. Then, at the focal point the entire beam has a diameter approximately λ. If this focal point is made to coincide with that for a much larger ideal lens or reflecting mirror of diameter D and focal length D or larger, the beam emerges from the latter with an angular diffraction width determined by its aperture, or λ/D. To obtain this result, it is not necessary actually to focus the beam to a small spot; this was assumed only for heuristic purposes. The limiting factors in achieving an intense, directed beam probably reside, not in the source, but in the more familiar technical problems of producing large mirrors of the required accuracy and controlling the optical distortions due to heating by the beam.

For the sake of discussion, two optical maser systems will be assumed with the following characteristics:

System (*a*). Power-level, 10 kW. continuous; frequency, ~ 5000 Å.; band-width, ~ 1 megacycle/sec. or 3×10^{-5} cm.$^{-1}$; diameter of reflector (D), 200 in. (maximum size of present telescopes); beam-width (λ/D), 10^{-7} radian.

System (*b*). A group of 25 masers, each of the same maser characteristics as system (*a*), but with an effective system aperture, D, of 4 in. (and therefore a beam width of 1 sec. of arc, or 5×10^{-6} radian). The entire group is to be pointed in the same direction within the accuracy of the beam-width.

The beam-width of system (*a*) could be attained in a system operating from a platform above (or in the absence of) a planetary atmosphere and of such accurate dimensions that diffraction is the limiting factor. (See following discussion.) When operating from within an Earth-like atmosphere, the atmospheric turbulence restricts the effective band-width to that which would be achievable in a 4-in. telescope system, suggesting system (*b*) in this case as a more reasonable choice.

* On leave from Columbia University, New York.

Detectability of Maser Signals

Two primary criteria for detection of a maser beam emanating from near a star are: (1) it must produce enough photons per unit area at the receiver to be detectable with a lens of practical size and in a reasonable time; (2) it must be distinguishable from the background of stellar light.

The maser system operated from above an atmosphere (system (*a*)) would produce a beam of intensity, I, where: $I = \text{flux}/\lambda(D)^2 = 10^{18}$ W./sterad. at 5000 Å. or, per wave-number: $I_\nu = I/\Delta\nu = 3 \times 10^{22}$ W./sterad. cm.$^{-1}$ in a band-width $\Delta\nu = 3 \times 10^{-5}$ cm.$^{-1}$.

The intensity of radiation from system (*b*) would be less by a factor of 100. Under the most favourable conditions, a star of magnitude 8·3 can be seen by the naked eye; hence, the system (*a*) beam could be seen by eye at 0·1 light-year. With ordinary binoculars against the normal sky, the range would be about 0·4 light-year. Corresponding distances would be less by a factor of 10 for system (*b*).

From a distance of 10 light-years, the system (*a*) could be seen visually through the Hale 200-in. telescope or could be photographed with ordinary techniques with an exposure of about 1 min. This time of detection gives about 10^6 quanta of signal, and presumably could be much shortened by special effort. The distance of 10 light-years is significant because, as noted by G. Cocconi and P. Morrison[1], there are seven stars of nearly the same luminosity and spectral characteristics as our Sun within this distance. System (*b*) would require correspondingly about a 1½ hr. exposure in the Hale telescope for detection at 10 light-years. Thus criterion (1) is well satisfied.

The beam intensities indicated here are quite sufficient to communicate between planets of our solar system. They must, of course, compete with a background of light reflected from the planetary surface. The intensity of sunlight scattered by the Earth's surface is less than $1/\pi \times$ cross-sectional area $\times$ solar constant $= 6 \times 10^{16}$ W./sterad., so that the maser beams could be easily seen against the background of the Earth as viewed visually through an optical filter a few hundred angstroms wide, or as a bright spot superimposed on the image of the planet in a telescope of moderate size. This affords an alternate communications technique with some advantages for specific cases over radio communications. For example, because of directivity, light could be beamed from Mars or the Moon to a particular part only of the Earth. Furthermore, equipment for receiving simple signals need not be much more than the human eye.

Consider now the question of detection of such a signal from a distant planet against the background of light from its star. There is some, but little, hope of resolving the two spatially. The Earth and Sun subtend an angle of about ½ sec. of arc at a distance of 10 light-years. Hence light of equal intensity from the two might be resolved at this distance by a telescope of very high quality. However, one can perhaps more easily resort to high spectral resolution in order to discriminate between maser and stellar radiation.

We may take the spectrum of our own Sun as representative of the light to be discriminated against. The intensity per unit wave-number of the continuum has a maximum near 5000 Å. of about:

$$I_\nu^*(5000\text{ Å.}) = 1{\cdot}2 \times 10^{21}\text{ W./sterad. cm.}^{-1}$$

with a total intensity:

$$I = 3 \times 10^{23}\text{ W./sterad.}$$

Here it is seen that the maximum stellar intensity per wave-number is 1·25 that of maser system (*a*) or about four times that of maser system (*b*). The band-width of 1 mc./sec. chosen for the maser might possibly be reduced to increase the relative intensity of maser to star, but possible difficulty in obtaining high-power masers with this stability and some other considerations which will be mentioned later make use of such narrow band-widths unattractive.

For the Sun, I_ν is lower than the value of 5000 Å. by more than an order of magnitude below 2500 Å. and above 15,000 Å., two orders of magnitude below 2000 Å. and above 4μ. Superimposed on this continuum is a discrete structure, the Fraunhofer absorption lines, and emission spectra in the far ultra-violet. The most pronounced absorption lines of Ca II, Sr II and Na provide windows several angstroms wide in which the intensity is less by an order of magnitude than that of the continuum. Of course, it is to be remembered that the Earth's atmosphere limits terrestrial observation to wave-lengths between 2900 Å. and some few microns.

A logical selection in transmission frequency would be either to use a frequency as far in the violet as atmospheric absorption permits, or to pick a prominent Fraunhofer line (as the Ca II *H* or *K* line). In either case, a gain by a factor of about 10–20 in the ratio is to be had over transmission at 5000 Å., the choice probably being dictated by the availability of a suitable maser material to produce the desired frequency. Were it only a question of the solar intensity, another two or three orders of magnitude could be gained by recording above the Earth's atmosphere in the 1400–1800 Å. region. However, the loss of reflecting power in mirror systems and the anticipated difficulties in maser operation at these wave-lengths make the region unattractive—even if recording above the atmosphere were not already too awkward. The advantages of transmission in the infra-red over that at 5000 Å. would be offset by the widening of the beam were diffraction the limiting factor as in system (*a*).

Assuming a maser system (*a*) operating, say, within the Ca II *H* or *K* absorption lines, the ratio of maser to Sun intensity is about 300 in the narrow band-width of 3×10^{-5} cm.$^{-1}$. A spectrometer with resolution comparable to 0·01 cm.$^{-1}$ (that is, somewhat better than a resolution of 10^6 at this frequency) would give a maser signal just equal to the stellar background. Present grating spectrographs of high speed and resolving power give a resolution close to this figure (for example, the echelle spectrograph of G. Harrison[2]). The use of interferometric techniques can provide a resolution of a few orders better than this. An instrument comparable to the coudé spectrographs developed for use in conjunction with the Hale 200-in. telescope and with the required resolution appears capable of producing an acceptable photographic image with an exposure of a little more than an hour. Much less resolution than 0·01 cm.$^{-1}$ would still yield signals detectable against background, although the maser signal would then not be so obviously narrower than some spectral emission lines.

Maser system (*b*) would give an intensity just three times that of stellar background, again in the band-width 3×10^{-5} cm.$^{-1}$. While convenient detectors operating within such a narrow band-width might be developed, none is yet available. A spectrometer of resolution 0·01 cm.$^{-1}$ would afford a maser signal 1 per cent as large as background, which might allow marginal discrimination.

One must consider the possibility that changes in Doppler shifts during the period of exposure will be larger than the spectral resolution used and thus weaken the image. The Earth's orbital or rotational motion, the orbital motion of a satellite around the Earth if such is used as an instrument platform, and corresponding motions of the transmitting source may all produce Doppler shifts which can change the frequency and smear out the maser signal. The maximum rate of variation of the fractional change of frequency due to a Doppler shift $\Delta\nu_D$ from a signal source following a circular path of radius r with angular speed ω is given by:

$$\frac{1}{\nu}\left|\frac{d\,(\Delta\nu)_D}{dt}\right|_{max.} = \frac{\omega^2 r}{c}$$

where ν is the frequency and c the velocity of light. Taking the motions within our own solar system as illustrative, one obtains maximum values of 2×10^{-10} per sec. for an Earth-based transmitter mainly due to rotation of the Earth and 10^{-11} per sec. for a Moon-based transmitter. For these Doppler changes on both the receiving and sending end of the transmission to be contained within the required limits of resolution of 0·01 cm.$^{-1}$, the times of photographic exposure in the visible spectrum, then, would be restricted to about an hour. This is, as already noted, the approximate time needed for a good spectrum if the transmitter were at a distance of 10 light-years. Alternatively, both sender and receiver might, of course, compensate for his own cyclical Doppler shifts, which would be well known to him.

The question of exposure, or integration time, has a different connotation depending on whether the observer is engaged in a search of the spectrum or has found a likely line. In the first situation, hundreds of angstroms of the spectrum can be examined in a single photograph and, consequently, the spectral search of a given star is not unduly hampered by fairly long times of exposure. The spectral line sought can be expected to be exceptionally narrow, at an abnormal frequency for the type of star in question, and varying in intensity. Observation of any of these characteristics should lead to closer examination. Once a likely line has been located, a photo-detection system of higher sensitivity could be used to reduce the required integration times to minutes for the purpose of recording modulations in the signal. Actually, with a 200-in. telescope and an efficient dispersing system, the modulation could be visible to the eye.

Discussion

Thus, it appears that if one postulates the existence of an optical maser system beamed towards us of the characteristics of system (*a*) at a distance of the order of 10 light-years, it is within the state-of-the-art for us to detect it. System (*b*) is marginally detectable, or detectable with good signal to background, if very narrow-band optical receivers are developed. One should hence consider the feasibility and expense of such systems as judged by our own experience, and of course in the light of any fundamental difficulties.

Advantages accruing from the coherence of radiation over a very large aperture, or from the theoretical possibility of obtaining coherence among several maser sources are nullified if the system is required to operate from within an Earth-like atmosphere. In this case, system (*b*) above, perhaps augmented in either power-level or numbers of system elements, appears most advantageous. An appreciable increase in the number of elements would not necessarily involve prohibitive expense. Accepting a criterion of minimum detectability as a signal of only 1 per cent of the background, system (*b*) as defined would be sufficient for the job. An added difficulty in working within an atmosphere should be noted. Local air turbulence caused by hot lens and mirror surfaces in contact with the atmosphere would widen the beam even more unless well controlled. The power density reflected from the mirror surface of system (*a*) is close to that of direct sunlight. Such problems, connected with handling a large amount of power in a carefully controlled optical system would probably be some of the most troublesome ones.

The unique advantages of maser sources can be better utilized in operation from a very high-altitude balloon, a space platform, or natural Moon—a possibility that may not have been seriously considered a few years ago but should be more acceptable to-day. The capability of the ideal system (*a*) could possibly be met by using a single large mirror, although the very large mirrors with which we have had experience have not attained the highest angular resolution possible (the Hale 200-in. has an angular resolution of about 1/3 sec. of arc (ref. 9)). The task of obtaining the limit imposed by diffraction may be a difficult one. However, the beam intensities of system (*a*) might also be met by a bank of smaller mirrors of higher accuracy, perhaps operated in phase (the beam intensity varies in such case as the square of the number). In this connexion, it should be noted that the 36-in. mirror to be used in the current *Stratoscope II* high-altitude balloon programme[10] is a casting of fused quartz which is expected to achieve its theoretical angular resolution of 1/10 sec. of arc.

It may be both an encouraging enlargement of possibilities, and at the same time an unwelcomed complication, to find that the frequency of the hydrogen line in the micro-wave region is not the only reasonable place at which to search for possible interstellar communications, and that the optical region also seems a logical one. What other methods are we overlooking which might appear natural to some other civilization? Far ultra-violet and infra-red are absorbed by most imaginable atmospheres friendly to life, and hence would be avoided unless reception above the atmosphere is to be expected. Beams of charged particles would be subject to inconvenient bending in interstellar fields. We see no way of producing neutron beams or electromagnetic waves much shorter than the ultra-violet[4] with adequate intensity. On the other hand, the rapid progress of science implies that another civilization, more advanced than ourselves by only a few thousand years, might possess capabilities we now rule out—they may have already been able to send us an exploratory instrumented probe. Since none has yet been seen, perhaps it would be appropriate to

examine high-resolution stellar spectra for lines which are unusually narrow, at peculiar frequencies, or varying in intensity.

Note added in proof. Dr. W. S. Boyle and Dr. R. J. Collins have independently arrived at similar conclusions (private communication).

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A PROPOSED DUAL NEUROHUMORAL ROLE OF ACETYLCHOLINE: ITS FUNCTIONS AT THE PRE- AND POST-SYNAPTIC SITES

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ACCORDING to the generally accepted concept of neurohumoral transmission, the arrival of a conducted nerve impulse at the presynaptic terminals of a cholinergic fibre causes them to liberate acetylcholine, which then diffuses across the exceedingly narrow (50–200 Å.) synaptic gap and combines with specific receptors at the postsynaptic site; the combination results in the production of a localized postsynaptic potential, which, if excitatory, triggers off a propagated nerve action potential[1]. In non-cholinergic fibres, other transmitter agents are considered to take equivalent roles; although several naturally occurring substances have been proposed as such, the only other neurohumoral agent which has been demonstrated reasonably convincingly is norepinephrine as the transmitter of the adrenergic postganglionic sympathetic fibres.

From the foundations laid by Loewi, Dale, Feldberg and their collaborators, subsequent work has largely confirmed the foregoing hypothesis. It has, moreover, provided the basis for explaining the mechanisms of action of several classes of drugs, particularly those acting on the peripheral divisions of the autonomic nervous system, its effector organs, and the motor end-plate of skeletal muscle. However, several observations in various laboratories, including my own, during the past few years, while not entirely inconsistent with the hypothesis, cannot be fully explained by it as presented above. The working hypothesis proposed here to explain these phenomena is that the acetylcholine mobilized by a conducted presynaptic impulse may act at two sites; postsynaptically, as outlined above, but prior to that at the presynaptic terminal itself, to bring about the release from the terminal of sufficient additional acetylcholine or of some other neurohumoral agent to initiate the characteristic postsynaptic effect. The proposed action of acetylcholine at its site of liberation is equivalent to its long-postulated role as a local hormone in smooth muscle and other tissues.

There is little claim to originality in the present proposal: it has been invoked in part before, directly or indirectly, to explain isolated phenomena. However, it is believed that the evidence which follows is now sufficient to present it as a general concept.

Histochemical Distribution of Acetylcholinesterase in Nervous Tissue

Determinations conducted on homogenates of various neural tissues have shown that, with certain exceptions, there is fairly good correlation between the concentrations of choline acetylase, acetylcholine and acetylcholinesterase, and that all three entities are present in relatively large amounts in cholinergic neurones (see ref. 2 for references). With the development of a microscopic histochemical technique for cholinesterases[2], and its subsequent modification to permit selective localization of acetylcholinesterase[3–5], it was possible to demonstrate that, in the cat, known cholinergic neurones (for example, anterior horn cells, preganglionic autonomic neurones) contain high concentrations of acetylcholinesterase throughout their entire lengths, whereas adrenergic neurones (for example, the great majority of those in the superior cervical and stellate ganglia) contain scarcely detectable concentrations. All the neurones of the parasympathetic ciliary ganglia are heavily stained for acetylcholinesterase; consequently, the small number of heavily stained neurones of the sympathetic ganglia were considered to be those giving rise to the cholinergic fibres to the sweat glands and the cholinergic vasodilator fibres. On the other hand, a limited number of cat sympathetic ganglion cells show intermediate staining, an observation which has been confirmed quantitatively by Sjöqvist and Holmstedt[6]. Likewise, the sensory neurones of the dorsal root ganglia, which are generally considered non-cholinergic, show intermediate grades of staining[5]. In the rabbit and monkey, in contrast to the cat, the differences between the autonomic cholinergic and adrenergic neurones are not nearly so pronounced; all the latter appear to contain relatively low but appreciable concentrations of acetylcholinesterase; again, concentrations in the sensory neurones in these species are intermediate[5]. The same situation was found in the brain of the rat[7]: all neurones giving rise to somatic motor fibres (for example, the hypoglossal nucleus) and parasympathetic preganglionic fibres (for example, the Edinger–Westphal nucleus) and those of certain correlation centres (for example, the amygdaloid

and caudate nuclei) were heavily stained; others (for example, the magnocellular division of the red nucleus) were practically unstained, whereas many (for example, the supraoptic nucleus and lateral thalamic nuclei) showed intermediate grades of staining. As a possible explanation for these observations, it was proposed a few years ago that the terms 'cholinergic' and 'adrenergic' might define the predominant, but not necessarily the exclusive, transmitting agent of a given neurone, and that those containing intermediate concentrations of acetylcholinesterase might liberate both acetylcholine and another transmitter[5].

Superior Cervical Ganglion

From the comparative effects of lipid-soluble and insoluble anticholinesterase agents, it has been shown that the neuronal acetylcholinesterase is separated by the cell membrane into external and internal fractions[8,9] and that transmission in the cat superior cervical ganglion is affected by inhibition of only the former[10]. At that site, the external, or functional, acetylcholinesterase is entirely presynaptic[11], in contrast to the neuromuscular junction, where most of the enzyme is postsynaptic[12]. From this it was inferred that acetylcholinesterase serves different primary functions at the two sites. In the course of an investigation of the physiological function of acetylcholinesterase in the ganglion, my colleague, Volle[13], determined the mean threshold doses of intra-arterially injected carbamylcholine and acetylcholine for producing postganglionic activation in series of normal and preganglionically denervated cats, both before and after inactivation of the ganglionic acetylcholinesterase by *di*isopropylfluorophosphate. To our surprise, the thresholds to both agents were markedly elevated by denervation; with carbamylcholine, a nearly thirty-fold elevation was evident prior to administration of *di*isopropylfluorophosphate, whereas a five-fold elevation in the acetylcholine threshold was unmasked only after inactivation of acetylcholinesterase. To explain these findings, we proposed that the threshold dose of acetylcholine or carbamylcholine in normal cats activated only the presynaptic terminals, causing them in turn to liberate acetylcholine immediately adjacent to the postsynaptic receptor sites, which in turn activated the ganglion cells. Following denervation, the higher thresholds were presumed to reflect those required for direct excitation of the ganglion cells. Consequently, it would appear that the primary function of the presynaptic ganglionic acetylcholinesterase is to limit the effect on the presynaptic terminals themselves of acetylcholine liberated there during transmission or the resting stage. Other investigators have published evidence of the susceptibility of the preganglionic terminals to activation by acetylcholine in pseudorabies-infected rats[14,15], and in normal cats[16], although the interpretation of the latter findings has been questioned[17].

Hypothalamico–Neurohypophyseal Tract

The work of Scharrer and Scharrer[18] and others has provided strong evidence that the hormones of the neurohypophysis are formed in the supraoptic and paraventricular nuclei of the hypothalamus, transported within their axons through the infundibulum, and stored until liberated in their terminations, the Herring bodies, within the neurohypophysis. From the work of Pickford and her associates[19,20], it appears likely that the hypothalamic control of neurohypophyseal secretion is regulated by cholinergic fibres. In an attempt to localize the cholinergic pathways involved, Abrahams[21], while visiting my laboratory, conducted a histochemical survey of the distribution of acetylcholinesterase in the hypothalamus of the dog. Unexpectedly, the enzyme was found in moderate concentrations only in the neurones of the supraoptic and paraventricular nuclei and their axons, and not in any of the presynaptic fibres adjacent to them. From the evidence cited earlier, this indicated that the only cholinergic neurones in the area of the hypothalamico-hypophyseal tract are the same ones which are assumed to elaborate the neurohypophyseal secretions. Among the suggestions offered at that time was that the same neurones might, indeed, liberate at their terminals both acetylcholine and the endocrine secretions, the latter under the influence of the former. More direct evidence of this possibility, and independent arrival at the same proposal, has recently been published from the laboratory of De Robertis. From an electron microscopic study of the neurohypophysis of the toad, these investigators discovered the presence in the neuronal terminals of two distinct populations of vesicles. Those of one group were dense to electrons, had an average diameter of 1150 A., and could be traced back to the hypothalamus; they were identified as the neurosecretory product. Those of the other group were considerably less dense, averaged 420 A. in diameter, and appeared only at the terminals; they were considered to be identical with the synaptic vesicles that have been described at various presynaptic sites[22], and may represent the storage form of acetylcholine and other transmitters[23]. Following this report, we have examined the neurohypophysis of the cat histochemically, and have found that the nerve fibres and associated Herring bodies stain consistently for acetylcholinesterase (Koelle, G. B., and Geesey, C., unpublished work). While indirect, the evidence is thus strong that the hypothalamico-neurohypophyseal fibres liberate both acetylcholine and endocrine secretions, and that the latter are under cholinergic control. In this situation, there is no participation of an immediate postsynaptic site.

Afferent Vagus

The primary sensory fibres are the only component of the peripheral nervous system for which a transmitter has not been identified. On the basis of their low contents of acetylcholine and choline acetylase, and the inconclusive effects of anti-cholinesterase agents on transmission[25], they are generally considered non-cholinergic. Matsumura, in my laboratory (unpublished work), has recently repeated the procedure developed by De Castro[26] for the establishment of functional re-innervation of the preganglionically denervated superior cervical ganglion by the afferent neurones of the peripheral vagus located in the nodose ganglion. Histochemically, the regenerated vagal fibres which synapsed with the superior cervical ganglion cells showed definite acetylcholinesterase activity, but were stained much less intensively than the normal preganglionic fibres. Ganglionic trans-

mission was potentiated by eserine. It was blocked by hexamethonium and tetraethylammonium, in the same dosage-range as produced blockading of intra-arterially injected acetylcholine; however, much higher doses were required to produce equivalent blockade in normal ganglia. While alternative explanations are equally likely, these findings are compatible with the proposal that acetylcholine normally takes an intermediate or subsidiary role in liberating another primary transmitter of the afferent vagal fibres.

Postganglionic Adrenergic Fibres

During the past few years, Burn and Rand[27–29] have developed an interesting new concept of the mechanism of action of tyramine, ephedrine and related non-catechol sympathomimetic amines. Stated in brief, they have obtained evidence that the major component of the action of such amines consists in the liberation of endogenous catecholamines from storage sites in the vicinity of the peripheral terminations of the postganglionic adrenergic fibres. Furthermore, they have shown that a cholinergic mechanism probably is involved in the liberation of catecholamines by the adrenergic fibres following their stimulation. Evidence for the latter phenomenon is based on two types of findings: following atropinization, the injection of acetylcholine or nicotine produces sympathomimetic effects at peripheral sites; after depletion of the peripheral stores of catecholamines by pretreatment with reserpine, stimulation of sympathetic nerves to many organs produces cholinomimetic effects. The location of the peripheral stores of catecholamines is still conjectural. Burn and Rand have considered both the terminations of the adrenergic fibres themselves and adjacent chromaffin cells as possibilities. Without excluding the likelihood of the latter, the former is consistent with the present proposal; it is strengthened by the finding of Burn and Rand that the stores are depleted of catecholamines following sectioning and degeneration of the sympathetic fibres. Again recognizing the possibility of alternative interpretations, this might then represent another example of the release of acetylcholine from axonal terminals in response to the nerve impulse, and its triggering in turn the subsequent release of the actual neuroeffector transmitter, norepinephrine, from the same terminals. It is interesting to speculate that this process may occur in the sympathetic neurones containing moderate concentrations of acetylcholinesterase, whereas the release of norepinephrine from those practically devoid of the enzyme may occur normally without the mediation of a cholinergic mechanism. Most of these points have been discussed by Burn and Rand[28].

Peripheral Terminals of Motor and Sensory Fibres

The terminations of somatic motor nerves have been shown to respond to injections of various cholinomimetic drugs by the discharge of antidromically conducted impulses, simultaneously with postsynaptic activation of the motor end-plate[30,31]. This might be construed as reflecting a physiological situation similar to that proposed for the superior cervical ganglion; that is, that normally the acetylcholine first liberated by the terminals promotes the liberation of additional acetylcholine from the same source to act as the transmitter of the neuroeffector.

More provocative is the question of the possible role of acetylcholine or a similar agent at the peripheral terminals of sensory fibres. It is well established that a great variety of sensory terminals or end-organs (for example, carotid chemo-receptors and stretch receptors, Pacinian corpuscles, taste buds) are activated by injected acetylcholine, and that this action is blocked by ganglionic blocking agents such as hexamethonium, tetraethylammonium, and nicotine[32]. However, it is a moot point whether this reflects the participation of acetylcholine in their physiological activation by normal stimuli[33], or whether it represents a purely pharmacological phenomenon[34].

Yet there is a remarkable parallelism between the events which occur at the dendritic terminals of crustacean stretch receptors[35], or at the Pacinian corpuscle[36], and those recorded at the motor end-plate in response to stimulation of the motor nerve fibre or local application of acetylcholine[37]. The initial response to pressure at the tip of the afferent fibre within the bulb of the Pacinian corpuscle is the development of a transducer or generator potential; this, like the end-plate potential at the neuromuscular junction, is relatively slow, graded, and is not propagated. At the region of the first node of Ranvier, the transducer potential triggers the propagated nerve action potential, just as the end-plate potential initiates the propagated muscle action potential. Hence, the transducer potential of the Pacinian corpuscle has the characteristics of a localized, chemically induced response. In their electron microscopic study of the corpuscle, Pease and Quilliam[38] noted that the enclosed nerve terminal contains inclusions similar to the synaptic vesicles found elsewhere at presynaptic sites. The sum of these observations leads to the suggestion that the normal mechanism for the initiation of the transducer potential, in response to pressure, may be the liberation of free acetylcholine or a similar agent by the same terminal on which it then acts. The nerve filament and central core of the Pacinian corpuscle of the cat have been shown histochemically to contain both acetylcholinesterase and non-specific or pseudocholinesterase[39], although the latter undoubtedly predominates[40,41]. A similar ratio for the two enzymes has been noted in the carotid body of the cat, in which the chemoreceptor cells contain considerable pseudocholinesterase and the nerve fibres a low concentration of acetylcholinesterase[4]. As in the terminals of the hypothalamico-neurohypophyseal tract, the Pacinian corpuscle represents a possible site of acetylcholine function where apparently no actual postsynaptic site is involved.

Conclusions

In the foregoing discussion, evidence from several lines of investigation has been presented in support of the proposal that acetylcholine, released at the presynaptic terminals by a nerve impulse, may have a dual role in synaptic and neuro-effector transmission: an action at the same site effecting the release of another transmitter, or possibly of additional quanta of acetylcholine, and a transmitter action at the postsynaptic site. This does not necessarily imply that acetylcholine plays any direct part in the propagation of the conducted nerve

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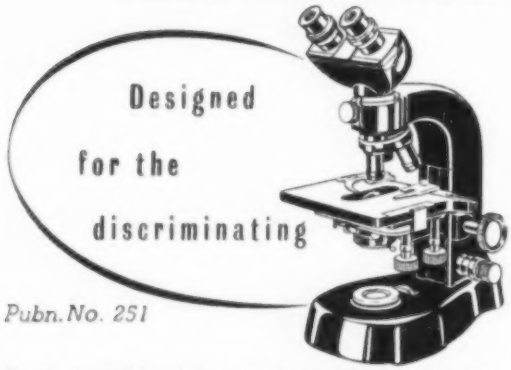

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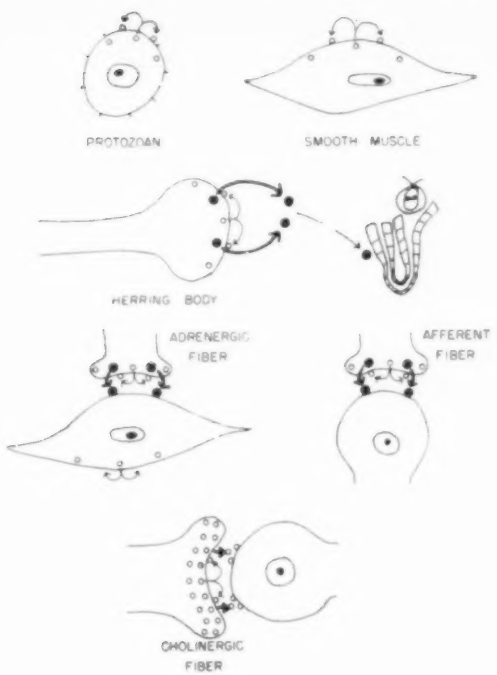

Fig. 1. Diagrammatic representation of the (1) direct influences of acetylcholine localized to its sites of liberation (protozoans, smooth muscle), (2) indirect influences through liberation of hormones acting at remote sites (from Herring bodies) and of neurohumoral agents acting at adjacent sites (from adrenergic and primary afferent fibres), and (3) direct influences at adjacent sites as a neurohumoral transmitter (from cholinergic fibres)

impulse, as proposed by Nachmansohn[42], nor does it preclude consideration of that possibility. The two actions considered here are presumably localized.

The postsynaptic transmitter role of acetylcholine seems now too well documented to require further discussion. There is also considerable evidence for its action at sites of release where no process of intercellular transmission is involved. The most direct demonstration of this phenomenon is in the ciliated protozoon, *Tetrahymena geleii*, which contains acetylcholinesterase, and in which acetylcholine appears to exert some control over ciliary activity[43]. Higher in the evolutionary scale, acetylcholine is involved in the beat of the cilia in the gills of the clam, *Mytilus edulis*; here, it is apparently formed by, and acts on, the ciliary epithelium without the intervention of any neural mechanism[44]. Likewise, in mammalian smooth[45] and cardiac[46,47] muscle, acetylcholine probably has a role as a 'local hormone', in that it appears to be liberated by the same muscle fibres on which it acts in the regulation of tone and rhythmicity, perhaps through modification of membrane permeability; superimposed on this inherent mechanism is the influence of acetylcholine liberated from the postganglionic parasympathetic fibres.

The proposed physiological activity of acetylcholine may be summarized in Fig. 1. At some sites, it has only a localized action on the cells in which it is formed, as in the last-quoted examples. Among such localized effects are included the liberation of secretory substances acting at a distance, as in the neurohypophysis, and, in the nervous system, of neurohumoral agents such as norepinephrine in adrenergic fibres, and perhaps an unidentified transmitter in the primary afferent fibres. In the so-called cholinergic fibres, sufficient acetylcholine is liberated, quite possibly in two steps, to act both locally, as above, and as the transmitting agent at the postsynaptic site. A universal role of acetylcholine at all synaptic and neuroeffector sites is not necessarily implied. In some cases, another agent or agents may have similar functions at the presynaptic site, just as other neurohumoral transmitters act postsynaptically where so-called non-cholinergic fibres are involved. Furthermore, the possibility is not excluded that a given fibre might liberate more than one transmitter acting post-synaptically, as previously proposed[5]. Finally, in isolated instances, synaptic transmission may occur without the mediation of a neurohumoral agent[48].

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THE GASSIOT COMMITTEE OF THE ROYAL SOCIETY AND METEOROLOGICAL RESEARCH

By Dr. D. C. MARTIN, C.B.E.
Assistant Secretary of the Royal Society

IN 1871, Mr. John Peter Gassiot conveyed to the Royal Society £10,000 of Italian Irrigation Bonds for the purpose of assisting magnetical and meteorological observations with self-recording instruments, primarily in the Kew Observatory. The Society set up its Gassiot Committee in the same year, and, apart from the Society's Sectional Committees, its Finance, Library and Scientific Relief Committee, it is one of the oldest of the Society's committees. The income of the Gassiot Fund has since 1871 been applied to the purposes set out in the Gassiot Trust Deed. Until 1910 the proceeds were passed first to the Kew Committee, then to the National Physical Laboratory Account of the Royal Society when the National Physical Laboratory had responsibilities in respect of the Kew Observatory. In 1910 the management of Kew Observatory was transferred to the Director of the Meteorological Office, with provision for scientific advice from the Gassiot Committee. Since 1920, when the Meteorological Office was incorporated into the Air Ministry, the income of the Gassiot Fund of the Royal Society has been paid annually to the Air Ministry on the recommendation of the Gassiot Committee in accordance with John Peter Gassiot's wishes.

In 1942, after consultation with the Air Ministry, it was agreed that the Royal Society should co-operate with the Meteorological Research Committee to assist the Air Council in the development of meteorological research on a wider basis and the Gassiot Committee was given terms of reference which included the following: (1) to advise the Royal Society on matters relating to pure research in meteorology and to supervise the disposal of such funds as may be made available by Council for this purpose; (2) to recommend as to the work of the meteorological and magnetic observatories with which the Society is connected; (3) to administer the Gassiot and other trust funds applicable to their maintenance. The Council of the Society asked the Committee to formulate plans for work on atmospheric composition, photochemistry, ultra-violet spectroscopy, synoptic meteorology and infra-red spectrometry. The Committee set up three sub-committees to assist it in encouraging this new programme of work, the sub-committees being entitled: (*a*) Atmospheric Composition and Motion; (*b*) Photochemistry of the Atmosphere; (*c*) Atmospheric Radiation and Temperature. With the aid of a grant, which was initially £5,000 per annum, and was later increased to £7,000 per annum, a worthwhile programme of work has been undertaken at a number of university centres. Among these were pioneering ozone studies by Prof. G. M. B. Dobson, at the University of Oxford, which have led to the creation of the permanent ozone survey service of the International Ozone Commission of the World Meteorological Organization; ultra-violet spectroscopic studies by Dr. T. W. Wormwell at Cambridge; infra-red work by Prof. P. A. Sheppard at the Imperial College of Science and Technology; research on molecular spectra by Dr. R. W. B. Pearse at the Imperial College; excitation of spectra by Sir Harrie Massey at University College, London; measurement of absorption cross-section by Prof. R. W. Ditchburn at the University of Reading; studies of airglow and auroral phenomena by Prof. D. R. Bates at the Queen's University of Belfast, and by Mr. J. Paton at the University of Edinburgh; and study of atmospheric winds by Mr. J. A. Ratcliffe at the Cavendish Laboratory, Cambridge. These studies have been carried out in close co-operation with various programmes of the Meteorological Office and Prof. T. G. Cowling of the University of Leeds, as well as Prof. D. R. Bates and others, contribute to the theoretical aspects of the work. Annually, the Gassiot Committee presents a report on its work to the Royal Society Council, and this report is forwarded to the Secretary of State for Air. From time to time, on the recommendation of the Gassiot Committee, special Royal Society discussion meetings have been held on subjects in the Gassiot programme. Prof. G. M. B. Dobson was the Committee's chairman during 1942–47, when he was succeeded by Sir David Brunt. Since 1952, Sir Harrie Massey has been chairman.

As early as 1953 the Gassiot Committee set up a small *ad hoc* sub-committee to consider whether atmospheric research, using rockets, might be initiated in Great Britain, and it organized a conference on the subject which was held in Oxford in that year. In 1955 a grant of £50,000 was received by the Royal Society from the Air Ministry for a programme of investigation of the upper atmosphere using high-altitude rockets. The Gassiot Committee created a new sub-committee to co-ordinate work at a number of university centres and to co-operate with the Ministry of Supply, particularly the Royal Aircraft Establishment. This programme, using *Skylark* rockets, has been very successful and has now been incorporated into the larger United Kingdom Space Research Programme which owes its beginning to the initiative taken by the Gassiot Committee in 1953.

During the past few years the organization of research programmes under the ægis of the Meteorological Research Committee has been re-organized, and some of the work hitherto conducted by the Gassiot Committee is considered to be more appro-

privately carried out directly by the Meteorological Research Committee itself through extra-mural contracts with university scientists. Some of those who have been supported in the past through the Royal Society will continue on the basis of such contracts and others wishing to carry out meteorological research should make application to the Director-General of the Meteorological Office, who is willing to support such research at university centres.

The Meteorological Office is, however, also anxious to continue its long and intimate connexion with the Gassiot Committee, and the Office recognizes that it provides an excellent medium for encouraging a wider interest in the problems of the atmosphere in universities, not least in subjects which border on meteorology. Arrangements have therefore been made for continued co-operation with the Meteorological Research Committee, it being agreed that the Gassiot Committee will concentrate its efforts on those problems of the physics of the atmosphere and allied subjects that are not at present dealt with by the Meteorological Research Committee. Initially, the Gassiot Committee, supported by an Air Ministry grant, will encourage further research in the photochemistry of the atmosphere and will promote, through discussion and other means, interest in other aspects. Close co-operation will be maintained with the Meteorological Research Committee by arranging joint meetings to discuss the Gassiot research programme. It is hoped that university physicists and others interested in its programme and not already in contact with the Gassiot Committee will approach the Royal Society.

The time-honoured association between the Meteorological Office and the Gassiot Fund, instituted in 1871, is to take a new form, which is warmly welcomed by the Royal Society. The Secretary of State for Air has approved the recommendation of the Meteorological Committee that two wholetime fellowships for research in the fields of seismology and geomagnetism respectively be established.

The income of the Gassiot Fund, now paid annually to the Air Ministry as mentioned above, will be regarded as a contribution to one of the fellowships, which will be tenable at Kew Observatory, and both fellowships are to be known as Gassiot fellowships, thereby preserving the historic connexion with John Peter Gassiot. The Royal Society Council accepted the invitation to nominate two representatives to the selection committee for these appointments, and Sir Edward Bullard and Sir Basil Schonland agreed to serve.

This story, which began ninety years ago, is an example of how a relatively small gift placed in the hands of a responsible body by a benefactor of science to encourage scientific endeavour has led to the development of a significant programme of co-operative research on a scale beyond his wildest dreams.

CARL LUDWIG GIESECKE (1761—1833)

By JOAN M. EYLES

SIR CHARLES GIESECKE, best known as a mineralogist, was born in Augsberg on April 6, 1761. His real name was Johann Georg Metzler, and his reasons for changing his name have never been satisfactorily established. He studied at Göttingen under J. F. Blumenbach, from whom he received his grounding in mineralogy. In his early years he was devoted to music and the stage, associating with Mozart, and taking some part in writing "The Magic Flute". This period of his life, perhaps some thirteen years, was mainly spent in Vienna. In 1794 he resumed his mineralogical studies, and travelled extensively to collect minerals, first in Austria and Germany, later in the Scandinavian countries.

In 1805, Giesecke was in Copenhagen, and was then commissioned by King Christian of Denmark to journey to Greenland to examine its minerals and prepare maps. He arrived in Greenland in 1806 and spent nearly seven years there. His private collection of minerals, which he had left in Copenhagen, was destroyed when the English navy bombarded the city in 1807. While in Greenland he discovered the famous cryolite occurrence at Ivigtut, on the Arsuk Fiord. Specimens of this rare mineral, a double fluoride of sodium and aluminium, had been sent to Denmark in the eighteenth century by missionaries, but the place from which they had been obtained was not known until Giesecke located it. This deposit later became of great importance to the aluminium industry. On his return to Denmark in 1813, Giesecke's ship called at Leith, and he spent some time in Edinburgh with Scottish mineralogists. Here he found some of the minerals that he had collected in Greenland. The ship in which they had been dispatched to Denmark had been captured by a French privateer, which, in turn, had been captured by an English frigate.

While in Edinburgh, Giesecke learnt that the Royal Dublin Society wished to appoint a professor of mineralogy. He applied for the post, and was elected by a large majority over several other candidates, although at the time he did not know enough English to lecture in the language—an indication of the esteem in which his achievements as a mineralogist were held. Giesecke held this post in Dublin until his death. In 1816, he was made a knight of the Danish Order of the Dannebrog, and became known as Sir Charles Giesecke. Thenceforward, apart from a brief return to Denmark and his native Augsberg between 1817 and 1819, he made Dublin his home. Here he lectured on mineralogy, arranged the valuable collections of the Royal Dublin Society, and also made mineralogical journeys into the west of Ireland. His published work relates mainly to Greenland and Ireland. He died suddenly in 1833, and the museum of the Society was closed for a fortnight as a mark of respect for his memory. His portrait, by Raeburn, was presented to the Society in 1817.

OBITUARIES

Dr. C. V. Drysdale, C.B., O.B.E.

Charles Vickery Drysdale, well known for his work on the design of electrical measuring instruments, died at Bexhill on February 7, at the age of eighty-six.

He was born in 1874, his parents being Dr. Charles R. Drysdale and Alice Vickery Drysdale. Like his father, his mother also was medically trained and was well known as Dr. Alice Drysdale Vickery (retaining her maiden name Vickery for professional purposes). She was born at Barnstaple, Devon, in 1846 and was fully trained in medicine and surgery for six years in London and Paris, but even in 1880 the British examining bodies refused to accept women. She went to Dublin, however, and obtained diplomas at King and Queen's College of Physicians certifying her as physician and licentiate in medicine and midwifery.

Dr. Drysdale was educated privately, and at Finsbury Technical College, and the Central Technical College, South Kensington. He was associate head of the Electrical Engineering and Applied Physics Department of the Northampton Institute (London) during 1896–1910.

He became a fellow of the Physical Society in 1898, and was a member of Council 1936–39 and Duddell medallist in 1935. He was also a member of the old Optical Society, of which he became president for 1903–4. A founder fellow of the Institute of Physics in 1920, he served on the Board during 1924–25 and was a vice-president during 1932–36 and editor of the *Journal of Scientific Instruments* during 1927–28. He was a Fellow of the Royal Society of Edinburgh and a member of the Board of Managers of the Royal Institution (1934–36). In 1920 he delivered the Kelvin Lecture on "Modern Marine Problems" at the Institution of Electrical Engineers, of which he was a member. He was honorary secretary of the Students' Section of the Institution of Electrical Engineers in 1894. He was also a Fellow of the Royal Statistical Society.

In addition to his scientific activities, Dr. Drysdale was a staunch member of the Malthusian League, of which he had been secretary, president and editor of the League's *Journal* during 1907–16. In 1921 and 1925 he had acted as president of Neo-Malthusian International Conferences in London and New York. He was a member of the Athenæum Club.

He was well known for his work on optical instruments, and for many years (1902–29) was examiner to the Spectacle Makers' Company. Such a wide range of interests is seldom found in one individual.

During 1910–16 Dr. Drysdale was closely associated with Mr. H. Tinsley, during part of this period in partnership, as makers of electrical measuring instruments. There he supervised the manufacture of many of his inventions like the a.c. potentiometer and the polyphase wattmeter, which are still made to-day as high-precision instruments. One of his great achievements was the phase-shifting transformer, the basis of servo-mechanisms in use throughout the world.

I first met Dr. Drysdale in January 1918 when he joined the staff of the Admiralty Research Laboratory at Parkeston Quay, Harwich. There he applied his wide knowledge of alternating current theory and electrical instrument design to Service problems. He designed sensitive mechanically tuned a.c. relays of sub-audio frequency, which could be actuated at a considerable range by the electromagnetic field surrounding a cable, lying on the sea bed, carrying alternating current of the same frequency as that of the relay. Afterwards (1919–21), at the Admiralty Experimental Station at Shandon (Gareloch), he made use of this system in the development of a 'leader cable' with visual indication on the bridge, to show the navigating officer the position of his ship, port or starboard, relative to the cable. Certain anomalies in this otherwise simple and useful system were observed, however, and this led Dr. Drysdale to make a very thorough full-scale investigation of the field distribution below and above the sea-surface around a submarine cable carrying alternating current. This work was done in Gareloch (off the Clyde) near Shandon and Rhu. The results of this important investigation, combined with those of theoretical and model-scale experimental work by S. Butterworth at the Admiralty Research Laboratory, Teddington, were published in the *Philosophical Transactions of the Royal Society* in 1924. This provided an explanation of the ambiguous indications of Dr. Drysdale's experimental leader cable. During the course of this research he became the first superintendent of the Admiralty Research Laboratory, Teddington, in 1921, a post which he held until 1929. In that year he was appointed director of scientific research, Admiralty, in succession to Sir Frank E. Smith. While serving in this post, in which he was in charge of all Admiralty research establishments, he was made a C.B. in 1932. He retired from Admiralty service in 1934.

He was a prolific writer, having published many original scientific and electrical engineering papers in *The Journal of the Institution of Electrical Engineers*, *The Electrician*, *The Proceedings of the Physical Society*, *The Journal of Scientific Instruments*, etc., as well as many contributions on Malthusian and Neo-Malthusian principles. One of his most important scientific papers is the one to which I have referred (*Trans. Roy. Soc.*) above. His book on *The Foundations of Alternating Current Theory* (published in 1910) was based on a series of lectures, extending over five years, which he gave at the Northampton Institute. This was one of the earliest efforts of which I am aware to emphasize the close analogy which exists in the theory of electrical and mechanical oscillations. At the end of the First World War he contributed to a collected work on *Mechanical Properties of Fluids*, in which he dealt with submarine signalling and the transmission of sound through water. His best-known book, *Electrical Measuring Instruments* (two vols.), in collaboration with Mr. A. C. Jolley, contains the work of many years study, theoretical and experimental, of the principles of design and operation of all kinds of electrical measuring instruments.

Dr. Drysdale lived a very full and energetic life, having a wide range of interests. He always took a great delight in seeing his theoretical deductions verified by an experiment. I remember him, however,

working on an experiment at the Royal Institution, after his retirement from the Admiralty, to demonstrate that the basis of Einstein's theory of relativity was wrong. At the time of his death he was busy writing another book.

In 1898 he married Bessie Ingram Edwards, who died some years ago. They had one daughter, Eva, who died young, and an adopted son, Eric, who is married and lives in South America.

A. B. Wood

Prof. A. H. Cox

The death of Prof. A. Hubert Cox on February 14, 1961, will be sadly mourned by his many students dispersed all over the world and by geologists in Britain and in Canada. After graduating at the University of Birmingham as a chemist, he studied in Strasbourg where he carried out research work on benzenoid compounds and a great variety of other chemical problems.

During the First World War he became engaged on chemical work of great national importance which ultimately caused him to turn from chemistry to mineralogy and finally to stratigraphic and structural geology. Even prior to becoming professor of geology in the University College of South Wales and Monmouthshire, he had carried out important research work on the Ordovician rocks of Wales. His enthusiasm and energy in tackling the difficult and unknown structure and petrology of Cader Idris became symbolic of his future interest in the geology of the Principality. His name will always be associated with the pioneering work that was done in the early part of this century on the older rocks of Wales and, in particular, with the establishment of type-sections in Pembrokeshire. Conscious of the contribution which geology and geologists should make to industry, he devoted himself to the problems connected with the development of the coals of South Wales. He was among the first to apply geophysical methods to the determination of geological structures, and his use of resistivity measurements in the Coal Measures became the basis for a great deal of the modern work in this field of geophysics. He was among the first to illustrate how resistivity methods could be used to locate water-saturated strata in the Coal Measures and how those could be used in the development of the mines. His earlier training as a chemist made him singularly able to conduct investigations into the incidence of silicosis, as it was then called, among the miners of the South Wales coalfield. So tireless were his efforts to secure knowledge of the environmental factors concerning this disease among miners and so conscious was he of his duty as a scientist to the community, that his work became responsible for the complete revision of the pensions schemes for miners afflicted with pneumoconiosis.

Likewise, his contribution to the welfare and the development of the University College, Cardiff, will always be remembered and revered, and very specially by the many students entrusted to his care. Through many of these he was able to make profound contributions to the understanding of the structure of the Canadian Rockies and more especially to that of the Selkirk Mountains. His arduous work helped to establish the location of several important reserves of gold and silver and he can be said to have been among the pioneers of the scientific development of the mineral resources of Western Canada.

W. D. Evans

NEWS and VIEWS

Director of the National Lending Library for Science and Technology: Dr. D. J. Urquhart

The Department of Scientific and Industrial Research recently announced that Dr. D. J. Urquhart has been appointed the first director of the National Lending Library for Science and Technology at Boston Spa, Yorks. Dr. Urquhart was educated at Barnard Castle School and the University of Sheffield where he graduated in 1931 with an honours degree in physics. Afterwards he obtained a Ph.D. in the Metallurgical Faculty at Sheffield, and then he worked in the research department of a steel works. In 1938, Dr. Urquhart was appointed to the staff of the Science Museum Library. During the War he was at the Ministry of Supply, engaged mainly in the technical administration of armaments inspection. In 1948, he was transferred to the Information and Intelligence Division of the Department of Scientific and Industrial Research, where he was responsible for the reorganization of the Headquarters Library and Records and carried out a number of surveys of the use made of technical literature in different industrial centres. In November 1956 he became responsible for planning the National Lending Library. Since then he has been wholly concerned with the planning and creation of the new library, which has included the introduction of Britain's Russian translating programme in co-operation with the National Science Foundation's programme in the United States. Dr. Urquhart writes frequently on library and technical information topics. In recent years he has made a number of notable contributions in this field, starting with a paper he read to the University and Research Section of the Library Association in January 1957 on the new National Lending Library. It was in this paper that Dr. Urquhart estimated the size and requirements of the National Lending Library, and forecast the huge growth of Chinese scientific literature in the future. He dealt with this subject again in a paper to the Library Association last year. In 1958, at the International Conference on Scientific Information in Washington, he reported the results of an interesting analysis of the pattern of borrowing from the Science Museum Library which has served to guide the acquisition policy of the National Lending Library.

Civil Engineering at Swansea: Prof. O. C. Zienkiewicz

Dr. O. C. Zienkiewicz, who has been appointed to succeed Prof. B. G. Neal (*see Nature*, **188**, 896; 1960) in the chair of civil engineering at the University College of Swansea, will bring to his new appointment experience of both British and American universities.

After graduating from the Imperial College of Science and Technology in 1943, Dr. Zienkiewicz conducted research into some problems of gravity dam design under Profs. A. J. S. Pippard and R. V. Southwell at the same institution. In 1945 he joined Sir William Halcrow and Partners, and for four years he gained experience in the design and construction of dams and hydro-electric projects. He was then appointed a lecturer in civil engineering at the University of Edinburgh where he remained until 1957, when he joined the staff at Northwestern University, Evanston, as an associate professor, becoming a full professor in 1960. Dr. Zienkiewicz's research interests have ranged widely, embracing both fluid mechanics and stress analysis. Apart from his work on gravity dams, several of his early papers were concerned with the behaviour of surge waves and with problems of hydrodynamic lubrication. His main interest at present is in the field of thermal stress analysis in elastic and viscous materials, and he is investigating applications to the design of concrete dams, reactor shields and other shell structures. Several lines of approach are being considered, notably structural models and analogue methods as well as analytical and numerical procedures. The building of new accommodation for all the Departments of Applied Science is to commence at Swansea in 1962. Dr. Zienkiewicz will therefore have the opportunity to plan further developments in civil engineering, specially suited to his own research interests, and he must also establish arrangements for teaching the much greater number of undergraduates to be admitted in the near future. His colleagues in this task will be Prof. R. H. Macmillan (Mechanical Engineering) and Prof. W. Fishwick (Electrical Engineering), now chairman of the Department.

Zoology at Ghana : Prof. E. E. Edwards

Prof. E. E. Edwards, who retired this year from the chair of zoology at the University College of Ghana, has become director of a new Entomological and Parasitological Research Unit under the National Research Council established by the Ghana Government in 1958. He will therefore be able to continue his interests in tropical entomology and parasitology which were a feature of the University Zoology Department under his professorship. He was appointed to Achimota, then the University College of the Gold Coast, in 1952, and during his occupancy of the chair was responsible for the planning of the zoological laboratories at the new Legon site of the College.

Prof. R. D. Purchon

Prof. R. D. Purchon, who has now been appointed to succeed Prof. Edwards, goes to Ghana from the chair of zoology at the University of Malaya in Singapore, which he has held for eleven years. During that time he established a very active school for the study of the animal ecology of Malaya, with particular emphasis on marine biology. Facilities for this type of work are already well founded in Ghana, where Accra has served as a centre for much of the previous work of the University College in this field.

British Participation in Space Research

In asking leave of the House of Commons on March 21 to introduce a Bill to provide for the establishment of a Minister of Space Research and Development, and for connected purposes, Mr. Woodrow Wyatt argued that no real progress in this important new field would be made until Britain had a Minister in the Cabinet responsible for co-ordinating everything to do with space. The Americans were spending £3 10s. a year per head of their population on space development, and the Russians an equivalent sum because they knew that the resultant advances in technology would be injected into other branches of industry. Britain, however, was spending not more than 1*d*. per head, and to fall 3 or 4 years behind in any department gravely handicapped technologists and made their task of keeping Britain in the forefront more difficult. Mr. Wyatt asserted that too many Ministries had a fringe interest and none an overriding concern in space matters, and that the Minister for Science was not sufficiently interested. He referred to the profit to be made out of communication satellite systems, but alleged that effort was being duplicated and that the Postmaster-General was indifferent to the work being done in this field by firms like the English Electric Co., Hawker-Siddeley, and Pye, and maintained that the future of Britain's export trade and her standard of living depended on not being left out of the space age. Leave to introduce the Bill was granted and the Second Reading ordered for May 5.

British Funds for Oceanographic and Hydrographic Research

At the Committee stage of the Navy Estimates 1961–62 in the House of Commons on March 14, several questions were raised on the vote of £21 million for scientific services, an increase of £1·7 million. This represents about 5 per cent of the Navy Vote of £400 million, but Mr. C. Ian Orr-Ewing, Civil Lord of the Admiralty, admitted that the true expenditure on research and development was considerably more, including expenditure incurred through the Ministry of Aviation. The 98-in. Isaac Newton telescope now being erected at Herstmonceux would cost about £780,000, of which half would come from Navy Votes and half from the Treasury, and it would not only be used by the Royal Greenwich Observatory, but would also be available for general use by other astronomers in the United Kingdom. Replying to specific questions about hydrographic work, Mr. Orr-Ewing said that R.R.S. *Discovery II* would cost some £570,000 this year, of which £285,000 would come from the Navy Vote and £285,000 from the Development Fund. Its maximum range would be 15,000 miles and its cruising speed would be 9–10 knots. It would be 260 ft. long with a loaded draught of 18 ft., and it was planned to have a scientific plotting room at deck-level; electronic hydrographic, biological, chemical and general laboratories, a low-temperature laboratory and an underwater instrument room with a trunk leading through the bottom of the ship. About the same amount as last year would be spent on research and development of nuclear propulsion, but there was a considerable increase in salaries, wages and allowances, resulting from adjustments to keep those of the scientific staff with salaries of scientists in industry and elsewhere. The vote included a grant-in-aid to the National Institute of Oceanography and a subscription to the International Hydrographic Bureau.

Water Research in Britain

In a written answer to a question in the House of Commons on March 20 regarding Department of Scientific and Industrial Research grants for research on the utilization and conservation of water supplies, the Parliamentary Secretary for Science, Mr. D. Freeth, said that direct expenditure in such research could not be separated precisely from that which had an indirect bearing on the subject. The best estimates of current expenditure (1960–61) by the Department and co-operative research associations were: Geological Survey and Museum, £32,350; Hydraulics Research Station, £93,100; Water Pollution Research Laboratory, £148,650; British Coke Research Association, £18,750; British Leather Manufacturers Research Association, £6,800; British Paper and Board Industries Research Association, £9,500; Water Research Association, £35,000; current grants to universities for special research work, £11,000.

Students Awards in Scotland

In a written answer in the House of Commons on March 28, the Secretary of State for Scotland, Mr. J. S. Maclay, said that, with the agreement of the local authority associations, from next October awards would be made by the Scottish Education Department to full-time university students, students training as teachers and students taking advanced full-time or sandwich courses at other establishments. Although the education authorities would no longer make the awards, their local officers would assist the Department by interviewing students and making local inquiries when questions of special difficulty arose, and they would be responsible for advising young people in their area as to facilities available for further education. They would continue to award bursaries to other further education students and to school pupils. There will be standard maintenance allowances for students to whom the Scottish Education Department made awards at the rate fixed for the university or college which the student actually attended. These rates have been fixed on an interim basis as announced on December 19, and it is intended to undertake a comprehensive review of the rates during the coming year.

The Match-making Industry in Britain

To mark their hundredth anniversary, the well-known match-making firm of Bryant and May has issued an attractive booklet which describes not only the history of the company but also changes in the way matches have been made over the years. Matches were invented in 1827 by an Englishman named John Walker, whose substances were: potassium chlorate, sulphide of antimony and gum arabic. A piece of fine sandpaper was included in each box. Herbert Spencer called this invention the greatest boon and blessing to come to mankind in the nineteenth century. Match-making materials have varied little since the time of the first British patent granted to Francis May in 1855. The head of the 'strike-anywhere' match contains chlorate of potash (to provide the oxygen) and sesquisulphide of phosphorus, while a safety-head match consists mainly of chlorate of potash and sulphur, providing flame when rubbed against the amorphous phosphorus on the side of the box. The materials in both heads are bound together by special Scottish glue. The sticks are treated with paraffin to help them burn and ammonium phosphate to prevent smouldering. A feature of the match industry is the curious way certain districts in Britain will buy certain types of matches—only the box is different—and no other.

U.S. Federal Expenditure on Science

In its ninth issue of *Federal Funds for Science*, the National Science Foundation analyses Federal expenditure on scientific research and development in the fiscal years 1959–61, during which period the total increased from 6,200 million dollars to 7,700 million dollars in 1960 and an estimated 8,200 million dollars in 1961; the corresponding obligations are 7,400, 8,600 and 8,500 million dollars, respectively, and of the last, about 10 per cent is for basic research (Surveys of Science Resources Series. Pp. iii+89. Washington, D.C.: Government Printing Office, 1960. 50 cents). As in 1960, some 90 per cent of the total is expected to be administered by the Department of Defense, the Atomic Energy Commission and the National Aeronautics and Space Administration. 44 per cent of Federal obligations for basic research in 1960 were allocated to educational institutions, 30 per cent to Federal agencies and 14 per cent to profit organizations. Obligations to the National Science Foundation increased by one-third in 1960 to 72 million dollars, and an increase to 84 million dollars is anticipated in 1961. Of obligations totalling about 1,900 million dollars for basic and applied research in 1960, the physical sciences, including mathematics and engineering, accounted for 56 per cent, the biological sciences for 27 per cent and the remaining 17 per cent went to the psychological, social and other sciences. Of this 'other sciences', about 85 per cent is accounted for by research into the space sciences administered by the National Aeronautics and Space Administration. Trends in expenditure and obligations over the period 1940–61 are also analysed in the report.

The Australian Scientist

It is a fair wind that finds among the farrago of scientific journals one that is devoted to science in its broadest fields. The tendency in the past has been for most countries to produce at some time or other a scientific showpiece, and it was logical that in time Australian scientists should wish to make their contribution. *The Australian Scientist*, a new journal (1, No. 1 (February 1961). Pp. 70. Subscription rates (1 year): Australia, Fiji, New Guinea, N… Zealand £A4 4*s*. 0*d*.; Commonwealth coun… (excluding the above) £Sterling £3 12*s*. 6*d*.; … Commonwealth countries £Sterling £4 5*s*. 0*d*. … hardt, Sydney: Tasman Productions, 9–23 … Street, 1961), does much more than ju… showroom for Australian science, and … major contribution to the communic… in general. As would be expected … editorial board, consisting of Prof… S. T. Butler, Dr. A. S. Fraser, Pr… Prof. H. Messel, Sir Mark … Robertson, Prof. R. H. Th… Wadham, the first issue set… of material and presenta… journal follows the trad… world's established … represent science it … planned that a s… commence as soo…

The first issue contains, besides the foreword by Dr. D. A. Cameron, Minister for Health and Minister in Charge, Commonwealth Scientific and Industrial Research Organization, a forthright article entitled "New Deal in Science Education", by Prof. H. Messel, and articles on mast cells, automatic computation, seashore life in Australia, genetics, civil engineering, cosmic radiation, plasma physics, the cyclotron, drugs and the heart, all by Australian authorities, and aimed at the greatest possible circle of readers. The outward appearance of the journal is most striking, and all articles are generously illustrated, and some even include a portrait of the author. While certain illustrations are much enhanced by colour, it does not seem that some warrant it (Figs. 4 and 5 on pp. 64–65), and their reduction to black and white would have, at least, done something towards lowering the cost of production and hence the price of the journal.

Birds killed by Poisonous Seed-Dressings

A REPORT, issued jointly by the British Trust for Ornithology and the Royal Society for the Protection of Birds, is presented in an *Intelligence Unit Bulletin* (No. 13, March 1961) issued by the Council for Nature, and provides firm evidence that many, if not most, of the large numbers of birds found dead in various parts of Britain in the spring of 1960 had been poisoned by consuming dressed corn either directly or by eating some other creature that had itself eaten the corn. The report lists 67 localities from Aberdeenshire to Kent in which dead birds were found; in 59 of these cases seed dressings are believed to have been the cause of death. Sufficient corpses were analysed to point to dieldrin as the seed dressing principally concerned. The most numerous birds reported dead were wood pigeons; there were almost as many pheasants, and smaller numbers of rooks, crows, chaffinches, partridges and blackbirds. Among insectivorous and predatory birds killed were two each of the tawny owl, buzzard and wren, and single specimens of the barn owl, lapwing and kestrel. A few mammals were also reported killed in the same way, among them three dogs, three cats, two hares and singletons of the fox, weasel and hedgehog. Fear is expressed that another great slaughter of birds is likely this spring, due to the heavy sowing programme which, as a result of the wet autumn and winter, farmers will have to undertake in the next few weeks. An appeal is made therefore to all naturalists to send information of any dead birds they may find to Peter Conder, Royal Society for the Protection of Birds, 25 Eccleston Square, London, S.W.1. The basic facts required are the date on which kills began, the numbers and species of birds and mammals involved, and the name of the seed dressing used nearby. One or two of the corpses of birds larger than pigeons, from each kill, would also be most useful for chemical analysis to determine the cause of death.

Nature Conservancy: New Appointments

LORD HURCOMB has been appointed chairman of the Nature Conservancy in succession to Mr. Arthur Bryce Duncan. Previously, Lord Hurcomb was chairman of the Committee for England, and is succeeded by Prof. A. R. Clapham. Lord Howick of Glendale has been appointed as a member of the Nature Conservancy. Sir Charles Connell, Prof. J. H. Burnett and Major S. F. Macdonald Lockhart have joined the Conservancy's Scottish Committee; the vacancies having arisen through the retirement of Prof. J. R. Matthews, Major D. C. Bowser and Mr. Michael Noble. Dr. A. M. Massee and Prof. D. L. Linton have replaced on the Committee for England Sir William Taylor and Dr. A. S. Watt, who have retired. On the Committee for Wales, Prof. P. F. Wareing and Mr. W. Vaughan Lewis fill the vacancies arising from the retirement of Prof. F. W. Rogers Brambell and Mrs. I. M. Vaughan.

The Textile Institute Scholarships

THREE scholarships are being offered by the Textile Institute: *The Textile Institute Scholarship*, which is a three years scholarship, total value £1,050, for the study of textile technology, and is open to young people who are, or have been, or intend to be, engaged in the cotton spinning or cotton weaving section of the textile industry in the United Kingdom; *The Peter Coats Scholarship*, which is for two or three years to the value of not more than £100 per annum, tenable at the textile department of any technical college in the British Isles, and is open to students who wish to take a course leading to a college diploma or other qualification in subjects connected with the cotton industry; *The Rowland Spencer Scholarship* is for training or research, to the value of £100 per annum, for persons already engaged in the textile industry and undertaking a part-time course at a recognized technical college. The closing date for applications for all scholarships is May 1, and application should be made to the General Secretary, Textile Institute, 10 Blackfriars Street, Manchester 3.

Gulbenkian Foundation Grants

THE trustees of the Calouste Gulbenkian Foundation of Lisbon have announced the grants, totalling about £550,000, made during the second half of 1960 (making a total of more than £1 million for the year). Of these, grants in the United Kingdom and British Commonwealth total about £70,000. Among the grants in aid of science are: £2,000 per annum for five years to the University of London Institute of Archæology (total £10,000) for the academic part of a postgraduate course in the care and restoration of ancient buildings; £2,000 for a gas liquefier for the Gulbenkian Radio-carbon Dating Laboratory, to the University College of Rhodesia and Nyasaland; £29,949 for cytological work at the Institute of Histology and Embryology, University of Lisbon; £3,750 to the Fondation Européenne pour les Echanges Internationaux to enable postgraduate science students to study in Portugal.

University News: Belfast

ADRIAN P. ROBERTS has been appointed senior lecturer in engineering mathematics. Mr. Roberts has been a lecturer in electrical engineering at the Imperial College of Science and Technology.

The College of Aeronautics, Cranfield

THE following appointments have been announced: *Lectureships*, E. R. Norster and J. H. Dunmore (aircraft propulsion); H. B. Gatland (electrical engineering); D. Hodgetts and G. H. Tidbury (automobile engineering). *Senior research fellowships*, Dr. G. T. Csanady (Department of Aerodynamics); Dr.

W. D. G. Bennett (Department of Ma
Research fellowships, D. Hyde (Depart
Flight); A. Kaye (Department of Materi

THE following appointments to lect
been announced: Dr. J. F. Bowers (m
Dr. A. Myers (physics); Mr. M. Well
computing).

DR. D. J. BOHM, Research Fellow in t
of Bristol, has been appointed to the Univ
of theoretical physics tenable at Birkbec
The following titles have been conferred:
reader in spectroscopy in the University of Lo
on Dr. Edna M. F. Roe in respect of her post at
Institute of Cancer Research: Royal Cancer Hospit
and that of reader in chemical pathology in the
University of London, on Dr. I. D. P. Wootton,
in respect of his post at the Postgraduate Medical
School of London.

Mr. Desmond Curran, senior psychiatrist at St. George's Hospital, has been appointed to the University chair of psychiatry tenable at St. George's Hospital Medical School. Mr. D. J. Wiseman, assistant keeper at the British Museum, has been appointed to the University chair of Assyriology tenable at the School of Oriental and African Studies. Dr. C. Long, head of the Biochemistry Division at the Institute of Basic Medical Sciences, has been appointed to the University readership in biochemistry tenable at that Institute.

Announcements

ANY material that has to do with the life of Alan Gregg, late of the Rockefeller Foundation, will be welcomed by his biographer. This should be sent to Dr. Wilder Penfield, Montreal Neurological Institute, Montreal, Canada.

THE annual conference of the Museums Association will be held in Plymouth during June 19–23, under the presidency of Dr. D. B. Harden. Further information can be obtained from the Secretary, Museums Association, 33 Fitzroy Street, Fitzroy Square, London, W.1.

A CONFERENCE on "The Control of Noise" is to be held at the National Physical Laboratory during June 26–28. Admission is by personal invitation and anyone interested should write to the Director, National Physical Laboratory, Teddington, Middlesex, from whom further information can be obtained.

THE Italian Society of Chemotherapy is organizing a symposium at the beginning of June. Among the subjects to be considered are: new penicillins; antitumoural antibiotics; activity and use of nitrofurane derivatives; radioprotective drugs. Further information can be obtained from the Secretariat of the Italian Society of Chemotherapy, Via Andrea del Sarto 21, Milan.

THE Northern Branch of Aslib is organizing a residential conference at St. Mary's College, University of Durham during April 20–22. To be included in the programme are a number of papers: "The Battle of the Books"; "O. and M. in the Library"; "The Function of the Library in Research Projects"; "The New University Library in Newcastle upon

A MEETING of the W
to be held on May 3, w
field meeting in the Abe
theme of "Glaciation as
Development" will be contin
tion of (*a*) soil profiles revealed
Forest and (*b*) cliff sections along
Aberystwyth towards Aberaeron.
be obtained from Mr. James A. Tay
of Geography, Alexandra Road, Aber

THE sixth Nuclear Congress, organize
Comitato Nazionale per l'Energia Nucleare,
held at the Palazzo dei Congressi, Rome,
June 13–18. Three symposia are being include
the programme: "The Thorium–Uranium Cycle";
"Nuclear Applications in Agriculture"; "Autoradiographic Techniques in Medical Science". A study day on "Conventional Engineering Problems in Nuclear Plants" is also being arranged. Further information can be obtained from Ufficio Stampa e Relazioni Pubbliche, CNEN, via Belisario 15, Rome.

AN informal discussion on the effects of ionizing radiations on organic and biological solids will be held at the Laboratoire de Chimie Physique, 11 Rue Pierre Curie, Paris Vème, during July 3–4, under the joint auspices of the British Biophysical Society and the Société de Chimie Physique. Information and application forms can be obtained from one of the organizers, Prof. J. A. V. Butler, Chester Beatty Research Institute, Fulham Road, London, S.W.3; Dr. L. H. Gray, Mount Vernon Hospital, Northwood, Middlesex, England; or M. Magat, 11 Rue Pierre Curie, Paris Vème, France.

THE name of T. Kobayashi (Japan) as one of the vice-presidents of the International Union of Geological Sciences has been omitted from a note appearing in a recent issue of *Nature* (April 8, p. 132).

PLANT VIRUS DISEASES

A GENERAL paper-reading meeting of the Association of Applied Biologists was held at the British Museum (Natural History), Cromwell Road, London, on February 10. Dr. C. Potter was in the chair. Although not advertised as a symposium it might well have been, for it had a coherent content of new and unpublished work on diseases caused by plant viruses in crops.

Several themes, apart from the obvious ones implicit in the titles, linked the different contributions. The first was the ubiquity of soil-transmitted viruses, some known and some suspected to be transmitted by nematodes. Another was seed-transmission which recurred in several contexts, and a third, carried or 'pick-a-back' viruses. These are viruses that cannot be transmitted alone by arthropods, but may be so in the presence of another virus that is transmissible by a vector.

All these aspects of transmission were mentioned in the first paper on "Some Celery Viruses", by Mr. M. Hollings (Glasshouse Research Institute). Among viruses isolated from celery crops was celery yellow vein, transmissible by grafting and by manual inoculation of infected sap, as well as through naturally infected soil. It reacts strongly to antisera prepared against a strain of tomato black ring virus, which is transmitted by seed, soil and probably nematodes. Cucumber mosaic and lucerne mosaic viruses were isolated from the field. A previously unrecorded virus, provisionally called celery yellow spot, could be transmitted from celery to celery only when cucumber mosaic was present; cucumber mosaic alone did not cause the symptoms, and yellow spot alone was not transmissible. Another previously undescribed virus, celery yellow net, was transmitted by grafting or manual inoculation only during the winter months; no aphid or other vector was found.

Mrs. M. A. Watson (Rothamsted Experimental Station) described carrot motley dwarf virus which causes a disease of carrots known to growers as purple top. In an experiment, infection in July caused a loss of about one ton per acre of carrots for every additional 15 per cent of plants infected. The willow-carrot aphid, *Cavariella aegopodiae*, retained the virus for many days when adequately fed on infected plants. Motley dwarf may be a complex of two viruses, motley dwarf proper and red leaf. Motley dwarf proper was transmissible by aphids and by manual inoculation to *Nicotiana* spp. but not by aphids thereafter. Red leaf has not been transmitted by manual inoculation, and does not seem able to infect *Nicotiana* spp. Possibly its presence enables motley dwarf to be transmitted by aphids, and it may be transmitted by seed in an attenuated form. Motley dwarf virus was infective in saps extracted with phenol, but infectivity was completely destroyed by addition of ribonuclease to a final dilution of 0·01 mgm./l., 3 min. before inoculation, suggesting that infective material in phenol extracts is nucleic acid.

Dr. J. A. Tomlinson (National Vegetable Research Station) showed that lettuce crops can be kept reasonably free from damage by lettuce mosaic virus in the summer, by sowing seed containing less than 0·1 per cent of seed-infection. In winter, cucumber mosaic caused a disease resembling that caused by lettuce mosaic. Cucumber mosaic is not transmitted by seed so control measures based on seed hygiene were less successful in winter than in summer. An unidentified virus caused symptoms similar to those of arabis mosaic when inoculated to *Chenopodium* spp., but was symptomless in lettuce.

Dr. R. Markham (Agricultural Research Council Virus Research Unit) presented a joint paper with Dr. R. MacLeod on "A Persistent Aphid-transmitted Virus Disease of Tobacco". This virus, provisionally called tobacco yellow net, was not manually inoculable, but was transmitted by *Myzus persicae*, which could retain it for several days after a single adequate feeding on infected leaves. It resembled the 'vein-distorting' component of K. M. Smith's tobacco rosette complex of viruses, and, like 'vein-distorting' virus, was able to act as a carrier for the other component of the complex, mottle virus, which was otherwise not transmissible by aphids. Yellow net might be easier to handle biochemically than other aphid-transmitted persistent viruses which usually have less amenable hosts than tobacco. However, vein-distorting virus, which it resembles, has proved disappointing in this respect.

At the afternoon session emphasis was on soil-transmitted viruses. Some of these, for example arabis mosaic, have previously been known to be transmitted through infected soil, but nematodes have only recently been shown to be the vectors.

Mr. R. M. Lister (Scottish Horticultural Research Institute), in a joint paper with Dr. A. F. Murant, described seed-transmission of arabis mosaic, raspberry ringspot and tomato black ring viruses in a wide variety of hosts, including many weeds. These viruses are disseminated by distribution of vegetative material from nematode-infested sites, but dissemination of infected seed may spread them even more widely. However, such spread is limited by the susceptibility of the wild plants to virus and vectors, and the amount of seed that becomes infected. Infected weeds may have poor ability to survive in competition with healthy ones and in cultivation. Even if they survive, it may be in sites free from suitable nematodes. These factors probably reduce the chances of virus being spread by seed transmission.

Speakers in the discussion also thought that the three viruses are mainly spread by infected propagating material, but the importance of the discovery that they are transmitted by seed was stressed. Mr. Lister mentioned that the viruses were pollen-transmitted, and distribution by pollen may be more effective than by seed.

Dr. B. D. Harrison (Rothamsted Experimental Station) gave a joint paper with Dr. R. D. Winslow on arabis mosaic virus. It included one of the first accounts of the behaviour of a nematode-transmitted virus in relation to its vectors. The virus has previously been associated with important diseases of raspberry, strawberry and cherry, very recently with white clover, marrow and celery. The patchy distribution of diseased plants in crops coincides with that in the soil of *Xiphinema diversicaudatum*, the vector of arabis mosaic virus. Adult nematodes usually transmit better than larvæ, but both are infective after being kept without plants for several

weeks. The virus remains viable a much shorter time *in vitro*, and must be in some way stabilized in the nematodes; possibly it multiplies in them. Galls that develop on roots of plants infested with *X. diversicaudatum* are caused by nematode feeding and not by virus infection. Evidence is accumulating that transmission of different nematode-transmitted viruses is specific to particular species of nematodes. Ecological studies showed that in some districts hedgerow plants are important hosts of arabis mosaic and of *X. diversicaudatum*, but in others the vectors, and probably the virus, are more widely distributed in the fields. An interesting discussion centred around the possibility that cultivation, and not preference of the nematodes for a particular environment, determined this distribution. A grass field that had not been cultivated for thirty years had nematodes only near its hedgerows, but Dr. F. Raw did not think thirty years to be a particularly long time for soil animals not to have returned after cultivation.

An important paper by Mr. R. Cropley (East Malling Research Station) described the identification and symptoms of viruses isolated from cherry trees with rasp leaf and leaf roll diseases which are widespread and damaging in sweet cherry orchards. Rasp leaf was found associated with raspberry ringspot virus, but the symptoms, of reduction in leaf size and rough enations on the backs of the leaves, can also be caused by arabis mosaic virus. Cherry leaf roll virus is readily transmissible by manual inoculation to many herbaceous hosts. Symptoms, thermal inactivation and particle size and shape are characteristic of soil, or nematode-borne 'ringspot' viruses, but leaf roll seems to be distinct from those already known. It is manually inoculable from cherry to *Prunus pennsylvanica*, and from tobacco to cherry and strawberry. Virus can be detected in young leaf tissues in the spring, but not in summer and autumn.

In the discussion Dr. Posnette emphasized the importance of cherry leaf roll; he thought that degeneration of orchards often attributed to age or poor husbandry was really caused by the virus. It was suggested that Tomlinson's lettuce latent virus (see paper No. 2) might be the same as cherry leaf roll virus.

An interesting symposium can be made to sound dull by the use of the dread word 'practical'. However, this series of papers gave information of practical importance to farmers and growers, as is only proper for applied biologists, but also contributed to general understanding of plant virus problems and reported advances of a more fundamental kind in virus research. There was clear indication of trends that could become important in the future.

MARION A. WATSON

PHYSICAL CONDITIONS OF SOIL

ON March 1 about eighty members of the National Vegetable Research Station Association attended talks and demonstrations on "Soil Physical Conditions affecting Plant Growth", given by the staff of the Chemistry and Irrigation Sections at Wellesbourne.

It is well known that the overall physical condition of a soil, often referred to as soil structure, and, in the surface layers, soil tilth, has considerable effect on the growth of plants. Furthermore, applications of bulky organic materials, such as farmyard manure and compost, have given yields of vegetables much higher than those produced by inorganic fertilizers alone. The general reason advanced for this difference is that the bulky organic manures improve the physical condition of the soil as well as providing plant nutrients. While many opinions have been expressed, in text-books and elsewhere, as to which of the soil physical properties are important, for example, water-holding capacity and aeration, there is still a dearth of experimental evidence on the relations between measurable specific physical properties of the soil and plant growth.

Experimental work in progress at Wellesbourne on the following subjects was described and demonstrated: soil aeration; soil moisture characteristics; the uptake of nutrients by plants, especially in the early seedling stage; the distribution and activity of the roots of crop plants; and the effect of soil physical conditions on the responses of plants to applications of irrigation water.

At present, there is no satisfactory method for measuring soil aeration, and hence there is no means of assessing the importance of this factor in crop production. The distribution of oxygen in a soil may affect plant growth by influencing the ability of plant roots to take up nutrients, and by altering the activities of the micro-organisms and thus the amount of nutrients available to the plant roots. Work, so far, has been confined to the latter topic. With the view of using the activities of the soil micro-organisms as indicators of availability of oxygen, the effect of oxygen concentration on them is being studied. Actively metabolizing micro-organisms in soil are covered with a thin layer of water which is exposed to the soil atmosphere. Since large differences exist between the oxygen concentrations at different points in the water layer, techniques have been devised which enabled the activities of the soil micro-organisms to be correlated with the oxygen concentration in the water at their surfaces. It has been shown that the respiration of the soil organisms and nitrification were not inhibited, and denitrification and anaerobic decomposition of soil organic matter were not induced, unless the concentration of oxygen at the microbial surfaces was less than about 10^{-6} *M*. Using microbial activities as indicators of oxygen concentration, physical theories of the distribution of oxygen in columns of moist soil crumbs are being tested, and efforts are being made to find out if it is possible to obtain the parameters necessary for the theories, from simple measurements on field soils.

In field experiments at Wellesbourne during 1954–61, applications of farmyard manure produced large increases in the yield of a wide range of vegetables. Measurements of the moisture characteristics of the manured and of the unmanured soils during the growth of a crop of leeks showed that at planting time in July the available water capacity of the two soils was the same, but by October the available water capacity of the manured soil was 24 per cent greater than that of the unmanured soil. Further, the extra water was held at tensions less than 0·33 atmosphere, and, therefore, would be expected to be readily

available to plants. These results could explain the large yield response of leeks to the application of farmyard manure which is especially marked in dry seasons.

The results of growth analyses of carrot crops grown with and without farmyard manure showed that, during the very early stages of growth, the rate of increase of dry weight was much greater on plots where farmyard manure had been applied, and that this initial difference could affect the final yield of the crops. Chemical analyses of the seedlings revealed differences in composition which were larger than might have been expected from the results of laboratory assessments of the available nutrients in the treated and untreated soils. Experiments on the uptake of nutrients by seedlings in the first five days after emergence have shown that the amount of potassium taken up during this period affects the rate of growth of the seedlings for about 35 days, irrespective of the potassium nutrient treatment given after the first 5-day period. While it appears that potassium was involved in the stimulation of growth of the seedlings on the farmyard manure-treated plots, the reason for the much greater uptake of potassium by seedlings on these plots is not known.

The effect of soil conditions on the distribution and activity of plant roots is important to the nutrient and water economy of the plant, but, unfortunately, there is little fundamental information on this subject. Some work has been done at Wellesbourne on the distribution of the root systems of various vegetable crops, and attention is now focused on devising suitable techniques for the investigation of the factors affecting root activities in defined soil systems.

In the midland, eastern and south-eastern counties of England, crop production is limited in four years out of five by insufficient rainfall. Irrigation is now widely practised in these areas and, in general, produces increased yields of most crops. However, the response to applications of irrigation water is affected by the physical condition of the soil, and on certain soils, notably silts and fine sands, yields can be decreased if irrigation water is applied in such a way that the surface of the soil is beaten down to form a 'cap'. Methods of irrigation to overcome this disadvantage are now being studied, together with the causes of the detrimental effect of the 'cap' on plant growth.

F. Haworth

SCIENCE AND EDUCATION IN COMMUNIST CHINA

In a paper presented to the American Association for the Advancement of Science at its New York meeting on December 27, 1960, Dr. T. H. E. Chen, describing the position of science and scientists in Communist China, explains that to the Chinese Communist science and politics were inseparable, and every scientist had to pledge himself unreservedly and unquestioningly to the Communist party: the study of politics and ideology was as important as the study of science. Ever since 1949, increasing pressure had been exerted on China's scientists to conform politically and ideologically, and scientists were required to follow the direction of the Communist party in their scientific work. Political interference was found in many areas and the idea of objective science was rejected. As regards the present position, Dr. Chen said there was a new interest in science and technology, and technical institutes at secondary and higher levels were producing large numbers of engineers, technicians and technologists. Better facilities for scientific study had been provided since 1956–57, living conditions and salaries for scientists had been improved, and laboratory and library facilities expanded. The predominant emphasis remained on applied science and technology and also violent opposition to science for its own sake. Moreover, scientists were so hemmed in by political restrictions and burdened with political requirements that there was little room for initiative and creativity. There had, however, been a mushroom growth of new ideas in technical innovations and improvements, but despite such spectacular results, much was lacking from the point of view of a long-range and balanced programme of scientific development. There was reason to believe, however, that beneath the outward conformity a good deal of resistance to Communist pressure still existed among scientists.

In a paper on the training, growth and utilization of scientific and technical man-power in Communist China, presented at the same meeting, L. A. Orleans, of the Library of Congress, reviewed briefly the educational system in Communist China, and especially its capacity to produce scientists and technicians, and then considered the professional man-power of China, its competence and the effectiveness with which it is used. Mr. Orleans stressed the importance of using with discretion data on Communist China. Despite some revolutionary educational reforms, the framework of the educational system is approximately that which existed under the Nationalist regime, but it is supplemented by a great variety of educational facilities which do, in fact, provide training in various subjects and skills with different degrees of complexity and intensity. Between 1949 and 1957 enrolment in primary schools increased by 40 million, in secondary schools by about 6 million and in institutions of higher education by 300,000; during 1958 enrolment in primary schools increased from 64·3 million to 86 million; in secondary schools from 7 million to 10 million; and in universities and institutes from 440,000 to 660,000; but inevitably the already inadequate education received by most pupils deteriorated further. The most glaring weakness in higher education is probably over-specialization: there is virtually no possibility of interchange among specialists, and in most institutions physics, for example, is no longer taught as a distinct and integrated subject. Despite the limited facilities, teachers and funds, the system provides a large number of people with an appreciation for education, and a relatively small number with the knowledge necessary to lead the drive towards industrialization and world status.

Mr. Orleans accepts the figure of 625,000 as most closely reflecting the number of persons with higher education at present living in Communist China, more than half of whom are under thirty years of age and almost 80 per cent are men. During the past few years the number of professional workers has been growing at about 10 per cent per annum, and under the Communists the greatest increase has

been in engineering, followed by education and agriculture. Of 170,000 with engineering degrees, 90 per cent have received them since 1949, while of 38,000 graduates in the natural sciences, two-thirds are Communist trained. Great inefficiency appears to exist in the estimates of future man-power requirements and in placing graduates. Most of the serious scientific work is being done in the Chinese Academy of Sciences, which in 1958 had almost 6,000 research workers (almost 75 per cent being assistants, trainees or technicians), and its affiliated institutes; even here scientific research was integrated with production. In 1958, the 650 research institutes in science and technology employed a staff of 82,100, of whom 18,100 were research and technical workers, 14,700 in industry and communications, 1,200 in agriculture and related fields and 2,200 in medical science and public health, but it cannot be assumed that all have completed professional training. Many engineering graduates are, in fact, little more than skilled technicians and many science graduates advanced laboratory technicians. China undoubedly possesses a limited number of first-rate scientists, but, at least in the immediate future, her achievements in science, as in overall economic growth, will depend on how much help is obtained from the U.S.S.R. More and more persons will graduate from the advanced institutions now established to train scientists and technologists, but their function must be problematic while China continues the policy of adapting present knowledge to immediate needs rather than sponsoring creative research.

TREATMENT OF RINGWORM BY GRISEOFULVIN

TINEA CAPITIS (ringworm of the scalp) is a dermatomycosis mainly affecting groups of children of school age. Although not serious, the disease is conspicuous, and affects the morale of children, keeping them from school and from participation in normal childhood activities. The bacterial complications to which it may give rise are sometimes serious.

The disease is carried home from school or from a group of playmates, and a reservoir of infection is then established among adults. In some communities in Israel, the proportion of adults suffering from ringworm is higher among women than among men. On the other hand, in Moslem communities it appears to be the men who maintain the disease and run the risk of serious infection, because of their custom of shaving their heads, which is frequently done without due attention to hygiene. Moslem women are protected by the care they give their hair.

Ringworm is particularly widespread in communities where life is organized around the family or the tribe or where people live together in crowded conditions. Some persons contract ringworm more easily than others exposed to the same risk, and the disease is more frequent among children suffering from protein deficiency. In the (then) Belgian Congo, Vanbreusghem examined thousands of children and found that its prevalence varied between 5 and 40 per cent. It was higher in areas where serious protein deficiency was known to occur and kwashiorkor was present. The same applied to cases treated in hospital: in Bukavu, 89 per cent of the children suffering from kwashiorkor were infected with ringworm. At present it is impossible to say whether this arises from a lack of vitamin A accompanying protein deficiency, a change in the sebaceous secretion of the scalp, or some abnormality of the skin or hair related to kwashiorkor and favouring the development of fungi.

In North Africa, in some parts of Central Africa, in the Eastern Mediterranean basin, in certain parts of the United States where there is a high percentage of Negroes, and in various parts of eastern Europe, ringworm may affect 30–40 per cent of the children. The health authorities of several countries have decided to attack this problem and the World Health Organization is giving assistance to the Province of Syria, the United Arab Republic and to Tunisia. In Yugoslavia, where a systematic campaign against ringworm is under way, the Organization has assisted a demonstration project of mass griseofulvin treatment, directed by Prof. E. I. Grin. The campaign being carried out and a general survey on ringworm and its treatment are outlined in a recent issue of the *WHO Chronicle* *.

The dermatophytic fungi (*Trichophyton*, *Microsporum*) live and multiply at the expense of the keratin they digest; as a result, the growth of the hair is impaired and it falls out, leaving bald patches.

The treatment used until quite recently consisted in desquamation of the parts affected so as to remove the diseased keratin, and the disinfection of the patches in order to prevent contamination of newly formed keratin. For this purpose, fungicidal ointments and pomades, and even X-ray therapy, which causes depilation, were employed. None of these methods gave reliable and permanent results. It was necessary to find a new treatment, acting internally instead of externally, that would enable keratin-producing cells to resist the fungus, and continue to resist it after they had become keratinized.

The discovery of griseofulvin provided an antibiotic satisfying these requirements. Isolated in 1939 from *Penicillium griseofulvum*, then from several other species of *Penicillium*, the antibiotic was identified chemically and used in horticulture against certain fungal plant pathogens. Its powerful fungistatic action attracted the attention of dermatologists, and, starting in 1958, investigations were carried out on its use in the treatment of certain human and animal dermatomycoses. The antibiotic gave better results than any form of treatment previously applied. It was more active when administered orally than parenterally, was not found in the serum of treated subjects, but, on the other hand, could be detected in their hair. In therapeutic doses it did not have any harmful or irreversible side effects. As a result of these outstanding properties it was decided to use it for mass treatment.

Following mass immigrations from highly endemic areas after 1948, ringworm, which had been almost unknown in Israel, again developed into a public health problem. The number of new cases reached 4,000–6,000 per annum. The good results obtained elsewhere with griseofulvin encouraged Israeli health authorities to adopt it for a mass campaign, after confirming its effectiveness and harmlessness in a

* *WHO Chronicle*, 15, No. 2: February 1961.

preliminary trial with a group of women and children in hospital at Tel-Hashomer.

Those most seriously affected are children aged 5–14 years. Although in most cases the condition clears up spontaneously at puberty, some victims bear the marks of the disease throughout their lives.

Trichophyton violaceum is the most widespread parasite; favus caused by *T. schoenleini* is also encountered. In the Arab village where the campaign was carried out there were 441 *T. violaceum* and 5 *T. schoenleini* cases. Griseofulvin was administered in single doses of 25/30 mgm./kgm. of body weight a day. At the end of three weeks there was a marked improvement in most cases. After eight weeks, 99 per cent of the *T. violaceum* infections and 60 per cent of the *T. schoenleini* infections were cured. All cases were cured after treatment for ten weeks. Twenty-five cases which were followed up after 2–6 months did not suffer any relapse.

DYNAMICS AND ENERGETICS OF SWIMMING IN WATER-BEETLES

By Dr. WERNER NACHTIGALL

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KINEMATIC and dynamic measurements[1] were carried out on *Acilius sulcatus* L. (Dytiscidae). The resistance coefficient c_w of the *Acilius* torso, as a criterion of its flow adaptation, amounts to 0·23 for a Reynolds' number, R_e of 5×10^3 to 8×10^3. Consequently, *Acilius* produces only 5·75 times as much resistance for a given velocity as a drop-shaped body of best adaptation, having a comparable frontal area, but only half as much as a corresponding ball. This very favourable value results from the dorsoventral flattening of the body, the greatest height of which lies in the front third and the greatest width in the rear third of the body, where the epipleura are pulled out so that the borders are sharp. There is no essential difference in velocity between dorsal and ventral flow, and there is no enlargement of the resistance coefficient by a smaller R_e as a result of the preformed places of vortex separations (Fig. 1). The body ends in a half-round edge; this hinders the vorticity of the plane separating dorsal and ventral flow. Measurements prove the hydrodynamic efficiency of this body-form; the resistance rises to about 120 per cent if the flow comes from behind, and to about 122 per cent if the edge is cut off. This body-form also possesses excellent swimming stability.

The single propulsion factor is the part of rudder-stroke force consumed by metapodial swinging that lies in the direction of movement, the forward drive. With each rudder-stroke, the forward drive impulse, I_R, that is, the time integral of the propulsive force during the rudder stroking, is reduced by the counter-drive impulse, I_V, which results from the forward pulling of the metapodials. The fraction of the total impulse available for propulsion, $\eta_i = I_R/(I_R + I_V)$, is the efficiency of underwater swinging as a propulsive factor. It can equal 1·0 in an ideal situation and it can be determined graphically in a complicated way for the stationary (η_{i1}) and freely swimming (η_{i2}) animal as follows: slow-swimming movement, $\eta_{i1} = 0{\cdot}84$, $\eta_{i2} = 0{\cdot}72$; medium-swimming movement, $\eta_{i1} = 0{\cdot}87$, $\eta_{i2} = 0{\cdot}78$; fastest-swimming, $\eta_{i1} = 0{\cdot}91$, $\eta_{i2} = 0{\cdot}81$. The η_i values for freely swimming animals are somewhat lower than for stationary ones, since the pulling forward of the metapodials happens in water which is moving in relation to the swimming animal. The faster the animal swims, the better is the efficiency; the greater the applied power, the better it is utilized. The levels of efficiency are surprisingly high with an average of 80 per cent. This is explained by the morphological and kinematic peculiarities of the metapodials.

In the rudder-stroke the surface of the leg, F, and the stroking speed, v, are large. Therefore, the induced resistance W, proportional to Fv^2, is very high. The leg stands with broad sides and with swimming hairs spread perpendicular to the direction of stroking; v is usefully maximal, when the leg is perpendicular to the median. During the 'partial thrust time' the expended force is changed in propulsion from 98 per cent to 100 per cent, and further to 70 per cent. The resulting harmful side-force amounts to a maximum of only 23 per cent of the forward drive.

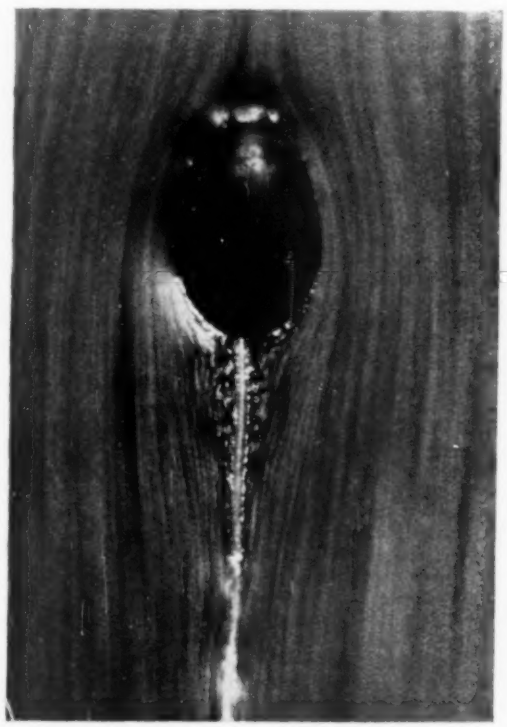

Fig. 1. *Acilius sulcatus*, L. Flow around the frontal area; taken with an associated reference system at $v = 35$ cm./sec. The laminar flow changes at the widest position of the torso into turbulence. The eddying (and therefore the resistance) is moderate ($R_e = 6{,}000$)

When the metapodials are pulled forward, v is somewhat smaller (an average of 90 per cent of the rudder-stroking speed); F becomes extensively reduced through the collapse of the swimming hairs and the forward-pulling of the leg close to the body, which first is turned around in the highly resistant rudder-position, when the body-speed has reached its minimum. Therefore, according to the above, the resistance generated by the forward-pulling of the leg is small; compared with the outstretched rudder-leg (100 per cent) it amounts to only 6·2 per cent by drawing after, 14·4 per cent by pulling forward close to the body and 31 per cent by turning into the new rudder-position.

The tarsus, also possessing swimming hairs, performs the chief propulsion, namely, 81·8 per cent of the total forward drive compared with 16·9 per cent of the tibia and 1·3 per cent of the femur. According to careful measurements, the part of total forward drive produced by the swimming hairs alone amounts to 67·7 per cent. Furthermore, they raise the forward drive of the solid leg to 230 per cent, the counter drive only to 45 per cent and consequently the effective forward drive to 300 per cent. Therefore, as 'split surfaces' they constitute an excellent rudder principle (Fig. 2). Besides, they move automatically and therefore they consume no muscle force. Moreover, through their uneven distribution, they turn the tarsus at the start of rudder-stroking automatically into working position. They occupy 79·8 per cent of the leg surface, and, with a 67·7 per cent total forward drive component, they attain 54 per cent of the forward drive of an equally large uninterrupted surface. They attain the basic advantage of their mobility and automatic movement as a result of their lattice arrangement with a loss of only 46 per cent of the forward drive against the theoretical maximum. The leg-thrust amounts to 480 per cent of the body resistance. So, for the *Acilius* torso, the rudder legs are very efficient locomotive organs.

The smaller the rudder-energy E_R, the greater is the energy available for other body-processes E_x, since the sum of these is equivalent to the total available energy, E. Only a fraction of the rudder energy E_R is used for the production of work, which is useful for locomotion, as a result of vorticity (η_1), through lateral drive (η_2) and counter-drive (η_3). It has been determined that $\eta_1 = 0{\cdot}50$, $\eta_2 = 0{\cdot}77$ and $\eta_3 = 0{\cdot}80$; consequently, the total level of efficiency, $\eta_{total} \approx 0{\cdot}30$. 70 per cent of the mechanical energy produced is lost in the leg movement itself. For a muscle efficiency, $\eta_4 = 0{\cdot}30$, becomes $\eta_{chem.} = 0{\cdot}10$. That is, the available chemical energy is transformed into work for locomotion to the extent of 10 per cent. Comparing the minimal chemical energy which is calculated for swimming at speed v with the total available energy which can be determined from respiration measurements at resting turn-over, it follows that *Acilius* expends 100 per cent when $v = 25$–30 cm./sec. (flight), 42 per cent when $v = 20$ cm./sec. (fast continual swimming), 2 per cent when $v = 7$ cm./sec. (slow continual swimming), only 5 per cent by normal distribution of movement and with a warm atmospheric condition; with a cool atmospheric condition it expends only 1 per cent of its available energy corresponding to the resting turn-over. This means that in daily life no notable energy losses result through locomotion ($E_x \gg E_R$; $E_x \approx E$), but, if necessary, extremely fast swimming is possible under optimal use of this great energy (flight, seizing of plunder; $E \approx E_R$). With *Paramecium*[2], the corresponding values amount to ½–12 per cent, with jumping grasshoppers[3] 100 per cent, and with running suckers[4] 60–100 per cent. With running insects they have not been investigated, but certainly they are less favourable. The quoted dynamic and energetic sizes present for the first time a quantitative idea of the excellent adaptation of water insects to the flowing medium.

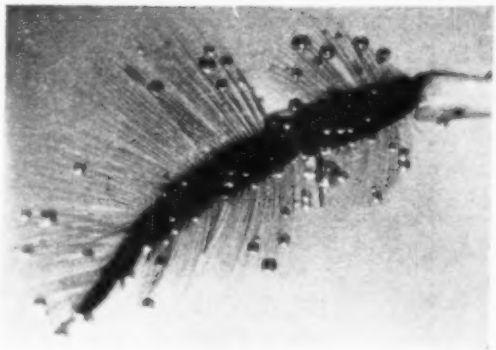

Fig. 2. Left metapodium of *Acilius sulcatus* L. at rudder stroking. The manner of the distribution of the swimming hairs and the spread, as also the enormous enlargement of the stroking area, are completely defined (taken in a flow apparatus)

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[4] Hempel, G., *Z. vergl. Physiol.*, **36**, 261 (1954).

COSMIC RAY AGES OF THE TREYSA AND SIKHOTE-ALIN METEORITES

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IT has been proposed[1,2] that the cosmogenic production-rate, dependent on depth, of stable nuclides in iron meteorites can be estimated from the measured rare gas ratios. One of the criticisms that has been directed at the scheme[2] is that (while it incorporated experimental data on the Sikhote-Alin and Treysa meteorites) different exposure ages were assigned to these meteorites; whereas, it is claimed, direct measurements[4,5] lead to approximately equal ages.

On re-examination of the data, an error was found in our calculation of the helium-3 production-rate in

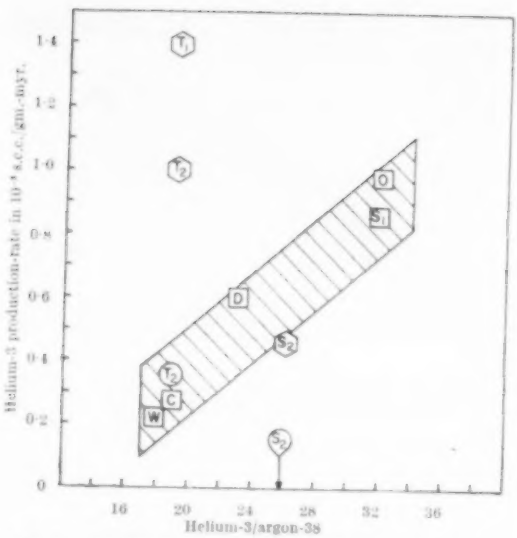

Fig. 1. Production-rate of helium-3 plotted against ratio of helium-3/argon-38. The squares are calculated from chlorine-36 data, the hexagons from argon-39 data, and the circles from tritium data. *O*, Odessa (ref. 10); S_1, Sikhote-Alin (ref. 10); S_2, Sikhote-Alin (ref. 4); *D*, Canon Diable (ref. 10); *C*, Carbo (ref. 10); *W*, Williamstown (ref. 10); T_1, Treysa (ref. 5); T_2, Treysa (ref. 4)

Treysa. The corrected scheme is shown in Fig. 1. New data on the tritium content of Treysa and Sikhote-Alin are included, although relative cross-sections for helium-3 and tritium production are not well known.

It is apparent that the scheme does not account for the argon-39 data on Treysa, nor for the tritium data on Sikhote-Alin. It has been pointed out[4] that no accepted model of cosmogenic nuclide production can account for the low tritium/argon-39 ratio in these two meteorites. It was suggested that diffusion loss of tritium is responsible for the anomalous value of this ratio. This suggestion is compatible with Fig. 1 for the low value of the tritium content in Sikhote-Alin, but not for the Treysa data (Sikhote-Alin is of the coarsest octahedrite structure, while Treysa is a fine octahedrite).

It is emphasized that Fig. 1 is merely an observation of an apparent correlation between radioactivity and rare-gas measurements. Future data may show the correlation to be coincidental or due to errors in measurement, in which case the scheme will be rejected. However, the low tritium/argon-39 ratio in Treysa may be due to an excess of argon-39. It has been noted[3] that, if one attempts to organize the rare-gas data for all the measured iron meteorites, particular ratios in particular meteorites seem to be anomalous. It was suggested that these anomalous values were due to secondary reactions on trace elements. For example, the excessively high value of the neon-21/argon-38 ratio in Tucson was tentatively ascribed to the $^{24}Mg(n,\alpha)^{21}Ne$ reaction, a larger amount of magnesium being present in this meteorite than in others. Similarly, the $^{39}K(n,p)^{39}Ar$ and the $^{42}Ca(n,2p)^{39}Ar$ reactions would lead to an excess of argon-39, and it is suggested that an excess of these elements in this meteorite may be the reason for the variation of the Treysa data from the proposed scheme.

In iron meteorites the argon-38/argon-36 ratio is generally about 1·6. In stone meteorites, with an iron/calcium/potassium ratio of about 100 : 6·5 : 0·4, the argon-38/argon-36 ratio reaches approximately 2, due primarily to the calcium isotopes. In Treysa this ratio varies from 1·52 to 1·75. This implies maximum calcium and potassium abundances relative to iron in Treysa of about 100 : 2 : 0·2. This limit does not prohibit the postulated argon-39 effect. Stoenner and Zahringer[6] have reported that the potassium content of iron meteorites may be extremely inhomogeneous; this may be a factor in the disparate values for argon-39 content of Treysa reported in refs. 4 and 5. Then a more nearly correct value for the exposure age of Treysa might be obtained by taking the nuclide production-rate from Fig. 1 than by using the argon-39 data.

Table 1. Cosmic Ray Age of the Treysa Meteorite, in Units of 10^8 yr.

Source of data	^3He–^3H	^{38}Ar–^{39}Ar	^{38}Ar–^{46}Sc	Only rare gases	^3He–$^3He/^{38}Ar$ (Fig. 1)
Ref. 4	1·0 (- -)	0·35 (0·45)			1·1
Ref. 4 (^{39}Ar) Ref. 5 (^{39}Ar)		0·25			
Ref. 4 (^3H, ^{39}Ar) Ref. 9 (^3He, ^{39}Ar)	1·4	0·49			
Ref. 5 (^{39}Ar) Ref. 9 (^{39}Ar)		0·35			
Ref. 5			1·2 (0·6)		
Ref. 9				(0·5 – 2·0)	1·5

Table 2. Cosmic Ray Age of the Sikhote-Alin Meteorite, in Units of 10^8 yr.

Source of data	^{38}Ar–^{39}Ar	^{38}Ar–^{36}Cl	^3He–$^3He/^{38}Ar$ (Fig. 1)
Ref. 4	0·22 (0·42)		0·17
Ref. 10 (^{36}Cl) Ref. 7 (rare gases)		0·17	0·15
Ref. 11		(0·12)	

In Tables 1 and 2 the exposure ages for Treysa and Sikhote-Alin are calculated again, using all available raw data on rare gas, tritium, scandium-45 and chlorine-36 measurements. The ages in parentheses are those deduced in the original papers. The differences arise because of the following considerations: (1) Fireman and DeFelice assumed an argon-38/argon-39 cross-section ratio of 1·5; recent data indicate a nearly constant ratio of about 2 from $0{\cdot}43 \times 10^9$ to 6×10^9 eV. They estimated a helium-3/argon-38 ratio of 20 for all iron meteorites; according to their estimate of the helium-3/helium-4 ratio, to Schaeffer and Zahringer[7], and to Vinogradov *et al.*[8], this should actually be about 26 in their sample of Sikhote-Alin. (2) Wanke and Vilcsek[5] used a value for the cross-section of argon-39 equal to 5 mb. Recent measurements indicate a value of 6·5 mb. at $0{\cdot}7 \times 10^9$ eV. rising to 12·4 mb. at 6×10^9 eV.; a value of 10 mb. was used here.

The spread in the ages listed in Tables 1 and 2 reflects both the different experimental values for measurements of the same nuclide in the same meteorite by different investigators, and the uncertainty in the assumptions necessary in proceeding from the measurements to calculations of the exposure

age. It is a measure of the errors involved, and would indicate that calculations, leading to such quantities as cosmic ray intensities from these data, contain an element of uncertainty. The ages proposed as 'best' are $0{\cdot}16 \times 10^9$ yr. for Sikhote-Alin and, for Treysa, $1{\cdot}3 \times 10^9$ yr. if Fig. 1 is used to estimate the nuclide production rate; $0{\cdot}35 \times 10^9$ yr. if the argon-39 data are accepted as indicating the primary flux.

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IMPULSE LOADING OF ROCK TARGETS TO PRODUCE FRACTURE PATTERNS SIMILAR TO NATURALLY OCCURRING RADIAL DYKE SYSTEMS

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DURING investigations of the impulse loading of rock and earth materials, a striking similarity was noted between fractures induced by impulsive loads in some rock types and the great dyke swarms occasionally encountered in volcanic provinces.

The impulse loading of a rock material can be accomplished in many ways. A simple method of delivering large amounts of energy to a small target area is to strike the target with a jet derived from a lined-cavity shaped charge. Such a jet-target impact creates a narrow empty hole in the rock target, referred to generally as a penetration. Under suitable conditions of target confinement, the penetration is accompanied by fractures filled or intruded by metal and metal oxides from the shaped-charge jet.

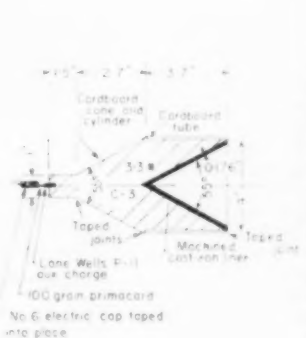
For fracture studies a jet was desired the metal fragments and oxidation products of which would contrast boldly in appearance with the target material. A light greyish-white limestone target rock was selected, previous experimental work[1] having indicated that limestone was an ideal target rock for fracture research. Thus, cast iron was chosen as the jet material because this metal appears dark in a light target, and in addition yields a dark grey-black oxide upon high-velocity impact. Such a colour contrast is especially important for fracture work. Those fractures definitely opened during and immediately following penetration are filled with liner metal and oxides, and are easily distinguishable from cracks created by handling the fractured target during its sectioning and study. Reliance on coloured fracture fillings means, however, that fractures that never were filled by metal and oxides are indistinguishable from both pre- and post-penetration cracks in the target.

To achieve high projectile velocities and obtain a large amount of target response to impact, heavy cast-iron liners were fired into limestone targets, with use of the simple lined-cavity shaped-charge design illustrated in Fig. 1. This charge design produces a 1-in.-diam. jet of small, sharp, cast-iron particles. The front tip of this heavy jet travels at a velocity of about 21,800 ft. per sec. (velocity across a course of 1·088 ft. extent; course located 2 ft. in front of the shaped charge). Fig. 2 is a flash X-ray photograph (exposure time 1 μsec.) of a cast-iron jet from a shaped charge of the type shown in Fig. 1.

Table 1. PROPERTIES OF THE MADERA LIMESTONE TARGET ROCK

Type of load		Sample cross-section (sq. in.)	Breaking strength (lb./sq. in.)
Tensile		0·05	500
Compressive		0·51	6,800
	Average	Larger grains mm. diameter	Smaller grains mm. diameter	Cement areas mm. diameter
Grain size	0·90	0·83	0·13	1·7

The targets used for this work were composed of relatively fine-grained, crinoidal Pennsylvanian limestone (Madera). Table 1 tabulates the physical properties of the target. Rock targets for impulsive-



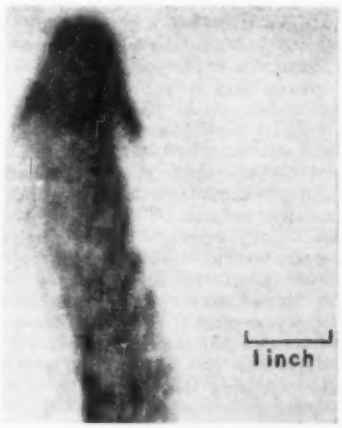


Fig. 1 (left). Design of the lined-cavity shaped charge used to form the fracture patterns shown in Figs. 3 and 4

Fig. 2 (right). A cast-iron jet derived from a charge of the design shown in Fig. 1 (exposure time 1 μsec.)

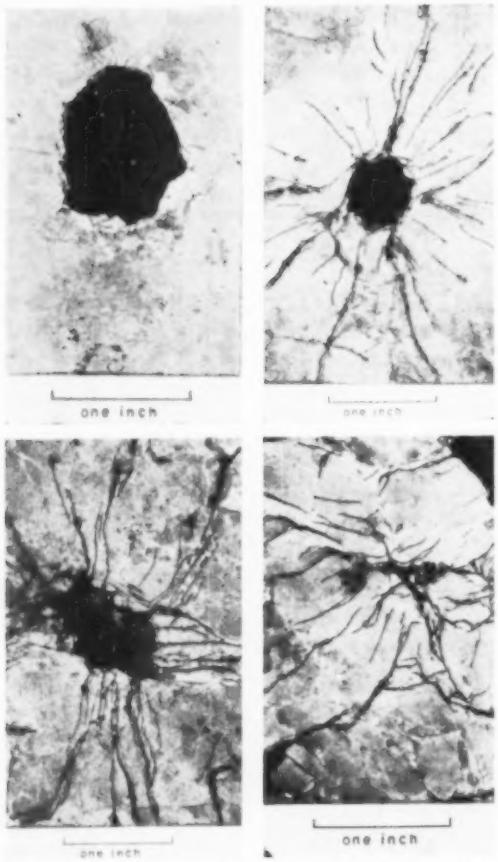


Fig. 3. (upper left) Result of firing a jet into a massive, uncracked limestone target; (upper right) the radial fracture pattern formed as a result of firing a jet into a cracked limestone target; (lower left) the typical fracture swarms formed at right angles to the walls of an angular penetration in a cracked limestone target; (lower right) the fracture complex formed beneath a penetration made in a cracked limestone target.

load investigations of the present type must not be permitted to break into a few large discrete fragments but must be kept essentially unbroken. To prevent fragmentation in a brittle target with such a low tensile strength as that of rock requires very massive targets or very heavy confinement. Massive limestone outcrops in place in the Earth's crust were used for the experiments reported in this article, making confinement laterally and into the target virtually infinite. Targets were able to expand only locally through the closing or tightening of pre-penetration cracks and joints, and perhaps to a minor extent through local decreases in porosity. Experiments so far suggest strongly that the presence of pre-penetration cracks is essential to formation of fractures intruded by jet metal and oxides. Where such cracks are lacking, no significant metal- or oxide-intruded fracture patterns developed in the targets.

Following the loading of the target to create a fracture system, a routine procedure was followed to prepare the target for study. Melted paraffin was poured into the target and allowed to solidify in order to preserve the detail of the penetration walls and help maintain the coherence of the fractured target. The paraffin was added, immediately following penetration of the target, while the target was still slightly warm. (Interestingly, rock penetrations are not hot but only mildly warm.) Next, a percussion-type rock drill was used to drill a double ring of holes surrounding the area of penetration and fracturing. Generally, in view of the type of jet used for penetration, a 1-ft. radius was used. The holes were drilled as close together as possible and slightly deeper than the expected depth of penetration. Following drilling the intervening rock was removed by hand to leave a cylindrical plug of rock containing the fractured area to be examined. Several holes were then drilled into the plug of rock at its point of attachment to the main rock outcrop, and the entire cylindrical plug was broken free as a single piece of rock. This was taken to the laboratory, where it was cut with a power hack-saw into a convenient rectangular block, mounted in plastic, and sawed into ½-in.-thick slices. The slices were made at right angles to the axis of the penetration, permitting the development of a rather complete three-dimensional picture of the target fracturing that accompanied the jet penetration.

Jet firings into limestone have so far illustrated three basic fracture patterns when the fractures are cut by a plane perpendicular to the axis of the penetration. These are: (1) penetration with essentially no fracturing; (2) radial patterns around a circular or elliptical penetration; (3) patterns with the fractures at right angles to the walls of a penetration having a rectangular or angular cross-section. No metal- or oxide-filled fractures occur in truly massive targets. Given a limestone with no pre-penetration cracks, and thus being unable to expand slightly about the penetration, no metal- and oxide-filled fractures will form. Simple metal- and oxide-filled radial fracture systems are found surrounding penetrations that occur in previously cracked

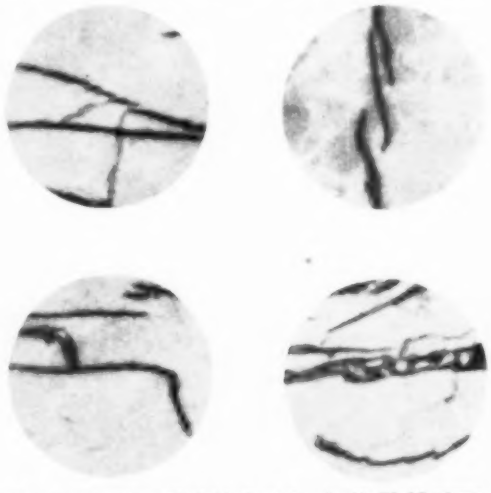


Fig. 4. Fine structure of individual metal- and oxide-filled fractures in a limestone target. The upper left photograph shows the microscopic en echelon character of macroscopically linear fractures; the upper right photograph shows macroscopic en echelon fracture alignment; the lower left photograph shows the typical abrupt junctions between fractures; the lower right photograph shows the rubble-filled character typical of relatively wide fractures

Fig. 5. The dyke swarms of the Spanish Peaks area in Colorado (western United States). Dark areas are intrusive centres, dark lines intrusive dykes. (Adapted from Knopf, ref. 2)

targets. In the case of a target with a pre-penetration crack cutting the penetration at an angle, fracturing begins on the side nearer the crack. In rocks with cracks scattered about the target area, relatively symmetrical fracture patterns are formed during the penetration process. Penetrations tend to become rather angular and irregular in outline towards their bottoms, instead of circular or elliptical. In the bottom areas the fractures resulting from the penetration process appear as swarms at right angles to the walls of the penetration. Although not examined in detail, the evidence at hand suggests that the fracturing immediately below a penetration is very complex. Fig. 3 illustrates the three types of fracture systems, as well as a section showing the complexity at the bottom of a penetration. Fig. 4 presents the fine structure of individual fractures.

Fig. 5 shows the great dyke swarm of the Spanish Peaks area in the western United States. A comparison of this figure with fracture patterns of Fig. 3 exhibits obvious similarity between the natural and artificial fracture-intrusion patterns.

In view of the foregoing similarities in fracture and intrusion patterns and the ease of formation of fracture patterns in rock models, I am continuing my work on the impulse loading of rock and earth materials.

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ACTIVATED NATURAL CRYSTALS

By Dr. GIOVANNA MAYR

Faculty of Medicine, University of Milan

SUCCESSFUL results have been obtained with tritium and carbon-14 [1] and also in experiments with lead[2], in which it was found that when a substance is placed in contact with a source in the form of a solid-labelled compound, the active substance can be found after some time at a distance from the source that cannot be explained on the basis of ordinary diffusion. These results suggested more general experiments to test the phenomena with other active sources and different kinds of substances for activation, particularly crystals.

The sources used were : calcium-45, carbon-14, phosphorus-32 and sulphur-35, prepared using materials supplied by the Radiochemical Centre, Amersham. The activity of each source was, at the beginning of the experiments, about 250 μc. As for the crystals, the inactivity of which was previously checked, in almost all the experiments slices were used about 2–3 mm. thick, cut in different directions ; in several cases it was also possible to make measurements of differently orientated slices cut from the same crystal. The specimens were : apatite (perpendicular to the z-axis and parallel to the same) ; calcite (perpendicular to the optic axis and parallel to a rhombic face) ; celestine (perpendicular to the x-axis and parallel to the same); gypsum (parallel to cleavage) ; pyrite (parallel to a cube face and parallel to a dodecahedral face).

The activation was produced by applying the slice of the crystal to the source for a time ranging from a few days to several weeks. At the end of the exposure the slice of crystal was taken off and counted on both faces, in some cases—when the activity was high—at a Geiger end-window counter ; in other cases at a gas-flow counter. In all cases activity was evident ; much stronger on the 'contact surface', that is, the face that had been kept in contact with the source, than on the 'opposite surface'.

The measurement of these activities was repeated at different times after the end of the exposure (several weeks and also several months). In all experiments done until now, activity was detected.

Besides this, the activated crystals were autoradiographed using Ilford G_5 nuclear emulsions ; a photographic effect was always noticed. Generally, the crystals were activated by exposure to a source, the active element of which was of the same chemical kind as some of the elements contained in the molecules of the crystal (apatite to calcium-45 and to phosphorus-32, calcite to calcium-45 and to carbon-14, gypsum to calcium-45 and to sulphur-35, celestine and pyrite to sulphur-35).

But an attempt was also made to expose a crystal to a source the active element of which was not of the same chemical kind as any of the components of the crystal molecule, but chemically allied to one of them, namely, celestine and calcium-45 ; in this case the effect was rather strong. A further attempt was made by exposing crystals to a source the active element of which was not of the same chemical kind as any component of the molecule nor allied to one of them, namely, gypsum and carbon-14 ; also in this case an activation effect, although a weak one, was noticed.

In order to check if the activation of the opposite surface was actually due to the presence of active

atoms and to obviate the effect of possible secondary radiation from the contact surface, the following procedure was adopted: two superimposed slices (cut from the same crystal and equally orientated) were exposed together; after removal from the source, the slice farther away was tested separately. In each case this showed a weak activity, and this could only be due to the presence of active atoms at a distance from the source corresponding to the opposite surface.

To check if the activity noticed at the opposite face of the activated crystal was due to active atoms having migrated from the contact surface through the crystal or along its surface, and to find out if, and how, the activity passed from the contact surface into the crystal, several crystals were carefully counted again, then weighed, ground on one face, weighed and counted again; this process was repeated several times and also on the opposite face. Care was taken during each grinding to renew frequently the material used for grinding and to clean thoroughly each ground surface before counting. This technique of grinding has been used in some work on ordinary diffusion[3], but the effect described here is different. In fact, the activity decreased with increasing depth from each surface, but the greatest decrease was noticeable only after the first grinding; after this, the rate of decrease was much lower and always less, the activity reaching a rather uniform value. This appears in Figs. 1 and 2, which relate to examples that illustrate the general result of experiments of this kind, and refer to the activity measured on both faces of slices of calcite cut perpendicular to the optic axis and cut parallel to a rhombic face.

These activities were measured some months after the end of the exposure and the measurements of the ground surfaces correspond to counts done as soon as grinding had been finished. The activity of the last two ground surfaces of each sample, after a lapse of time, appeared to have increased (probably lattice disorders had occurred during grinding).

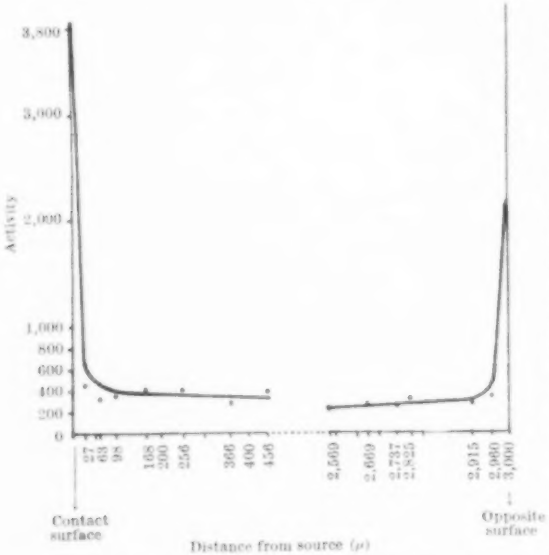

Fig. 1. Calcite cut perpendicular to the optic axis. Distance from source represents distance from contact surface. Activity is net counting-rate ± *S.D.*

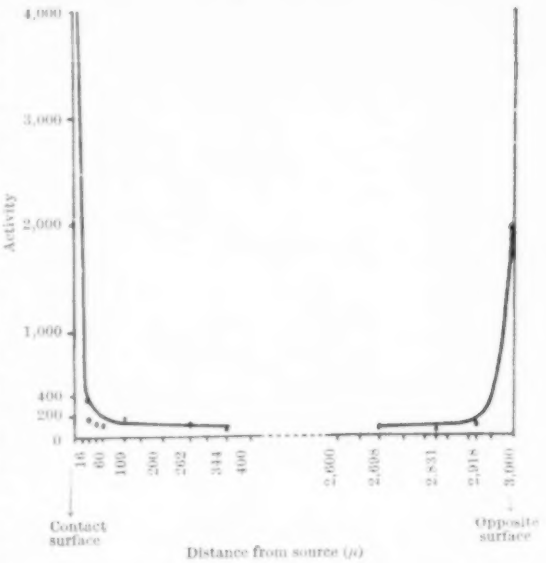

Fig. 2. Calcite cut parallel to a rhombic face. Distance from source represents distance from contact surface. Activity is net counting-rate ± *S.D.*

The result of the experiment demonstrates that the active substance penetrated into the crystal; at the same time the particularly high activity noticed at both external surfaces of the slices demonstrates that some active substance also migrated along the surface. The magnitude of this effect, calculated on the basis of the activity in the region where it appeared to be more or less sufficiently uniform, assuming that the activity measured corresponds to the radiation emitted from a depth of 150 microns (about three-quarters the range of the beta radiation from calcium-45 in calcite) and correcting for self-absorption, was: 0·0064 μc./gm. (in the first sample with calcite perpendicular) and 0·0022 μc./gm. (in the second sample with calcite parallel).

The difference cannot be ascribed to the different directions alone, since geometry and exposure time were also different.

It has been demonstrated that natural crystals can be activated by simple contact with a radioactive source. It appears that the active atoms migrate and that this effect may be considered as the combination of two effects: (1) a migration through the material in depth (bulk effect); (2) a migration along the surface (surface effect). This effect may be explained by the fact that the radioactive substance present in the source produces an excited state: (*a*) in the source itself by means of the radiation emitted and of the recoil of the emitting atoms; (*b*) in the contacting substances by means of the radiation up to its full range (a region that can be called 'range layer').

Consequently, in the source and in the contacting substances, up to the range layer, breakage of bonds, ionization and knock-on and knock-off of atoms may occur. These facts explain the possibility of atom exchange between neighbouring molecules and, in solids, the production of lattice defects (vacancies and interstitials). This, together with the possibility of intergranular migration, opens the way to a further

migration beyond the range layer, which differs from ordinary diffusion, because the concentration at the origin, instead of being constant, increases with time.

A theoretical treatment of these processes, done in collaboration with someone else, leads to conclusions in agreement with the experimental results and will be published separately. Obviously, not only the active atoms migrate, but also all kinds of atoms and ions that have undergone collision, and this may occur from source to contacting substance as well as vice versa.

Therefore, the active element observed in the active crystals by counting will be mixed most probably with the inactive carrier in the same proportion as in the source itself, so that it may be expected that, until saturation is reached, the magnitude of the effect may be proportional to the square of the specific activity of the source.

The effect here described differs from ordinary diffusion, not only because it is explained differently, but also because the experimental conditions are completely different, as neither particularly adherent contact nor heating is required. Further differences concern its magnitude and the two kinds of migration.

The experiments done up to now are not sufficient to give a complete picture of the effect on crystals, but are sufficient to indicate some lines of research : (*a*) The dependence of the effect on the chemical constitution of the source and of the activated substance, as well as on the lattice conditions ; also dependence on crystallographic structure. (*b*) The explanation of some concentric arcs which were noticed on some autoradiographs. I shall be pleased to hear from others who have done experiments of this kind.

This research has been carried on in the Department of Radiotherapeutics of the University of Cambridge. I thank Prof. J. S. Mitchell for hospitality and advice; also Dr. N. F. M. Henry, of the Department of Mineralogy, who kindly read the manuscript of this paper. Also, I thank the Consiglio Naz. le delle Ricerche, which gave grants for my stay in England.

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PATTERNS OF PREFERENCE IN EQUIPROBABLE SITUATIONS

By Prof. JOHN COHEN and PETER COOPER

Department of Psychology, University of Manchester

WE have previously[1] distinguished two types of gambling situation. In one, the player's skill may, if he so decides, affect his success or failure ; in the other, his skill (or what he believes to be his skill) is confined to making the choice, and once his choice is made, he is unable to do anything to affect the outcome. This second type is the characteristic lottery situation and the one with which we are now concerned. The earlier work was limited to isolated choice situations and not properly systematized. This defect may now be remedied by introducing a new method of representation or 'model'.

All variations of the sorts of choice we propose to study may be represented by assigning suitable values to the symbols :

$${}^{r}_{s}D^{w}_{l}$$

where D is the number of draws which the subject can make from a given source (s); w is the number of winning tickets ; l is the number of non-winning tickets; s is the number of sources of tickets ; and r indicates that a ticket drawn from a given source is replaced at random before the next draw.

The experimental procedure required the subjects to choose one of two (or more) possibilities of winning a prize. For example, they could choose to draw once from a box containing ten tickets including one winning ticket, *or* from a box containing a hundred tickets including ten winning tickets : ${}_{1}1^{1}_{9}$ or ${}_{1}1^{10}_{90}$. The instructions varied appropriately from one situation to another. More than six hundred subjects, young and old, took part in these experiments.

Let us now consider the results of the systematic experimental variations in turn :

(i) *Effect of varying 's'* (that is, number of sources or boxes from which the tickets were to be drawn).

The subjects were presented with the following four alternatives:

$$ {}^{r}_{1}10^{10}_{90} \text{ or } {}^{r}_{s}10^{10}_{90} \qquad (1, a)$$

where s took the values 2, 5 or 10.

$$ {}^{r}_{1}10^{10}_{990} \text{ or } {}_{10}10^{10}_{990} \qquad (1, b)$$

$$ {}_{1}1^{1}_{9} \text{ or } {}_{2}1^{1}_{4} \qquad (1, c)$$

$$ {}^{r}_{1}10^{10}_{90} \text{ or } {}_{20}10^{10}_{40} \qquad (1, d)$$

In a further experiment subjects ranked the following situations in order of preference :

$$ {}^{r}_{1}10^{10}_{90},\ {}^{r}_{5}10^{10}_{90},\ {}_{10}10^{10}_{90},\ {}_{20}10^{10}_{40} \qquad (2)$$

The general result was to prefer the alternative with fewer sources. In 1,041 choices, some 68 per cent preferred the alternative in which the ticket was to be drawn from a single source ($p < 0{\cdot}01$).

(ii) *Effect of varying w and l* (that is, the number of winning and non-winning tickets).

Three situations were examined, when p, the mathematical probability of drawing the winning ticket, was 0·1, 0·5 and 0·9 respectively, namely :

$${}_{1}1^{w_i}_{l_j} \text{ or } {}_{1}1^{10}_{90}$$

where i, j take the paired values 1,9; 2,18 or 5,45

$${}_{1}1^{w_i}_{l_j} \text{ or } {}_{1}1^{50}_{50}$$

where i, j take the paired values 5,5; 10,10 or 25,25 and

$${}_{1}1^{w_i}_{l_j} \text{ or } {}_{1}1^{90}_{10}$$

where i, j take the paired values 9,1; 18,2 or 45,5

A preference (statistically significant) was displayed for choosing from the larger total of tickets $(w+l)$, when p was 0·1, and from the smaller total when p was 0·5 or 0·9.

(iii) *Effect of varying D* (that is, the number of draws).

The principal choice situations here were :

$$ {}_1 1^{w_i}_{l_j} \text{ or } {}_1 10^{l_i}_{w_j} $$

where i, j took the paired values 1,9 or 10,90.

The preferences for one or other alternative seemed to be unstable from group to group except when the number of draws was counterbalanced by a larger value of w, in which case there was a tendency to prefer the latter.

(iv) *Effect of varying the mathematical probability of drawing the winning ticket as well as the value of the prize, proportionately.*

Here the choice was short odds ($p = 0{\cdot}1$) of winning a prize (box of chocolates) or long odds ($p = 0{\cdot}01$) of winning ten boxes. The preference was clearly in favour of the shorter odds. When shillings were substituted for chocolates in another experiment, the preferences for short odds virtually disappeared.

(v) *Points of subjective equivalence of w, l and D.*

From additional data provided by our subjects, it was possible to determine the mathematical probability of drawing a winning ticket when values of w, l and D in the rejected alternative were changed by the subject so as to render the latter as attractive as the chosen alternative. The inference is justified that winning tickets, non-winning tickets and draws are not subjectively valued equally when each is adjusted for equivalence to either of the others in the accepted alternative. Thus the psychological probability attached to draws is less than that attached to winning or non-winning tickets; and assessments of l are more realistic than assessments of w or D.

(vi) *The problem of transitivity of preference.*

When our subjects' preferences are studied over sets of different choices, some 15 per cent appear to be intransitive in the strict sense. In fact, however, the psychological value or 'utility' of any alternative is not constant but may vary according to the alternative with which it is juxtaposed. It follows, therefore, that the use of a notation which suggests invariance (A is preferred to B, B to C, therefore A to C) would be a misapplication of the principle of transitivity. Thus, for example, ${}_1 1^1_9$ may be preferred to ${}_1 1^{10}_{90}$ because of a smaller l; and ${}_1 1^{10}_{90}$ may be preferred to ${}_1 10^1_{90}$ mainly because of a larger w. But ${}_1 10^1_{90}$ may still be preferred to ${}_1 1^1_9$ because of the larger D.

General conclusions.

The notation we have introduced enables the experimenter to represent a great variety of situations and also facilitates the interpretation of the results. Two generalizations may be hazarded :

$$ {}_r D^{w_i}_{l_i} \text{ is preferred to } {}_{ns} D^{w_j}_{l_j} \quad (1) $$

when $l_i > w_i$, $l_j > w_j$, $l_i > l_j$

$$ {}_s D^w_l \text{ is preferred to } {}_s D^{nw}_{nl} \quad (2) $$

when $p > 0{\cdot}1$

These may be explained on the ground that when the chances of success are smaller than the chances of failure, the majority of our subjects concentrate on the possibility of winning. They prefer, therefore, to rely on a concentration of winning tickets in fewer sources; and they prefer a large aggregate of winning tickets to a small aggregate of non-winning tickets.

When, however, the chances of success are equal to or greater than the chances of failure, most of our subjects concentrate on the alternative with an absolutely small number of non-winning tickets. They prefer to rely on a dilution of the non-winning tickets in a larger number of sources, and they prefer a small aggregate of non-winning tickets to a large aggregate of winning tickets.

When $w = l$, the choice situation clearly discriminates between two types of person: one with a desire to maximize the chances of success and the other with a desire to minimize the chances of failure. This discrimination may prove to have important diagnostic value in clinical psychology and studies of 'personality'.

In general, the preferences seem to be based neither on the relative values of D, w and l nor on their absolute values, but on some combination of relative and absolute values. This is consistent with the results of our earlier quantitative studies of meaning[2]. Such preferences may reflect a combination of relative and absolute psychological phenomena which have hitherto been regarded as autonomous (for example, in Weber's law and the perceptual constancies). This and other theoretical questions of choice in equiprobable situations will be discussed in a full report of the investigation to appear elsewhere[3].

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A PHYSICAL THEORY OF CARCINOGENESIS BY AROMATIC HYDROCARBONS*

By Dr. J. B. BIRKS

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A NUMBER of aromatic hydrocarbons can induce cancer when injected into or painted on to the skin of a mouse. These compounds, which are also carcinogenic in other sites and in other animals, have been called primary carcinogens[1] to distinguish them from the secondary carcinogens, such as the 4-aminostilbenes and azo-compounds, which are more specific in their biological activity, and which probably act through metabolites.

It is observed that there is a significant correlation between the carcinogenicity index and the energy E_1 of the 1st excited π-singlet state of the molecule[2]. An analysis of data[3] for 66 hydrocarbons and 1 : 2-benzanthracene derivatives is shown in Fig. 1. It is found that 22 of the 23 carcinogens considered have $E_1 = 3{\cdot}04 - 3{\cdot}20$ eV. (24,800 – 25,950

* Paper read at a meeting of the British Biophysical Society, London, December 1960.

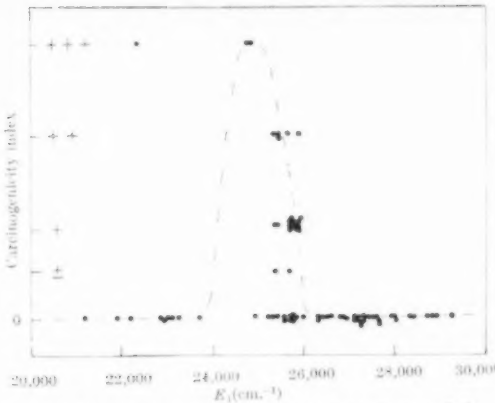

Fig. 1. Polycyclic hydrocarbons and 1 : 2-benzanthracene derivatives. Carcinogenicity index versus energy E_1 of 1st π-electronic singlet state

cm.$^{-1}$). On the other hand, 12 of the 43 non-carcinogens considered also have E_1 in this 'active' region. The degree of correlation indicates that E_1 is related to the carcinogenicity, but that additional factors, such as protein affinity, may also enter.

The form of Fig. 1 suggests a resonance between the carcinogen molecule and some cellular constituent. A common intermolecular resonance effect observed in aromatic molecular systems is dipole–dipole transfer of π-excitation energy, the theory of which has been formulated by Förster[4]. The rate parameter for dipole–dipole energy transfer is determined by the overlap resonance integral :

$$J = \int f_d(\lambda)\ \varepsilon_A(\lambda)\ \lambda^5 d\lambda \qquad (1)$$

where $f_d(\lambda)$ is the quantum intensity of fluorescence emission of the sensitizer molecules, and $\varepsilon_A(\lambda)$ is the molar extinction coefficient of the acceptor molecules at wave-length λ.

E_1 is the edge of the 1st singlet π-electron absorption band, which has a mean energy $\bar{E} \simeq E_1 + 0{\cdot}5$ eV. Hence if the carcinogenicity is plotted against $\bar{E}$ a similar curve to Fig. 1 is obtained, but with its peak at $\bar{E} \simeq 3{\cdot}54$ eV., corresponding to a mean absorption wave-length $\lambda \simeq 350$ mμ. The one important cellular constituent known to emit efficiently in this spectral region appears to be the essential amino-acid, tryptophan, the emission spectrum[5] of which with a peak at $\lambda = 348$ mμ is shown in Fig. 2.

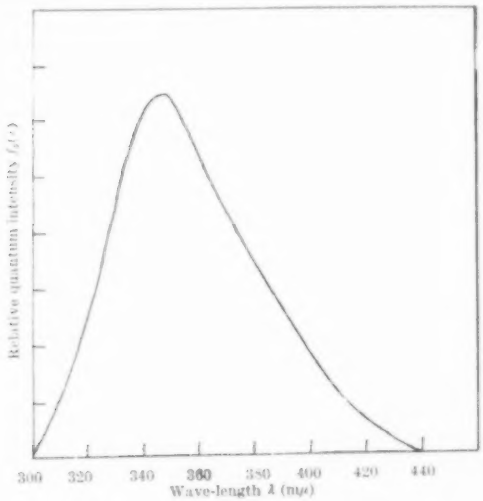

Fig. 2. Fluorescence spectrum of tryptophan

To test the hypothesis that carcinogenesis may be due to dipole–dipole resonance between tryptophan and the carcinogen molecule, as suggested by the above considerations, the overlap integral J has been evaluated, with tryptophan as the sensitizer and the hydrocarbon as the acceptor, for the polycyclic hydrocarbons and 1 : 2-benzanthracene derivatives the absorption spectra[6] of which are known. The results for the methyl derivatives of 1 : 2-benzanthracene are shown in Fig. 3, in which the carcinogenicity index (mean of the Pullman–Pullman[7] indices for painting and injection) is plotted against J, measured in arbitrary units.

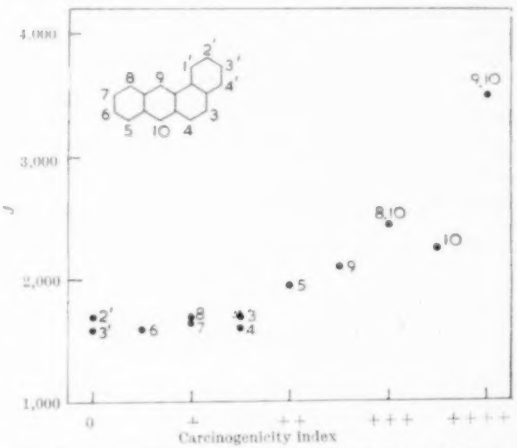

Fig. 3. Monomethyl and dimethyl derivatives of 1 : 2-benzanthracene. Tryptophan overlap integral J versus carcinogenicity index

The methyl 1 : 2-benzanthracenes, which vary markedly in biological activity, have always proved the most challenging and critical group of compounds in previous attempts to correlate some physico-chemical property with carcinogenicity. Pullman and Pullman[7] agree that their electronic theory fails to account for several differences within this group, and they enumerate many other physical and chemical properties that show much less satisfactory correlations. Considering (*a*) the uncertainties in the carcinogenicity data, (*b*) that no allowance has been made for differences between $\varepsilon_A(\lambda)$ and $f_d(\lambda)$ in solution and in the cellular environment, and (*c*) that no account has been taken of the protein affinity of the hydrocarbon, the monotonic relation between J and the carcinogenicity index shown in Fig. 3 is striking. The structurally related potent carcinogens, cholanthrene (++++) and 20-methylcholanthrene (++++), also have high values of $J = 2{,}250$ and $J = 2{,}200$ respectively, consistent with those of the methyl-1 : 2-benzanthracenes.

Heidelberger and Moldenhauer[8] have shown experimentally for a number of aromatic hydrocarbons that the formation of a stable complex with mouse-skin proteins is a necessary, though not a sufficient, condition for carcinogenicity. The outstanding exception

to a simple correlation between protein binding and carcinogenic activity is 1 : 2 : 3 : 4-dibenzanthracene, which although non-carcinogenic is as tightly bound as the potent carcinogen, 3 : 4-benzpyrene. The absorption spectrum $\varepsilon_A(\lambda)$ and the 'tryptophan overlap' spectrum $f_a(\lambda)\ \varepsilon_A(\lambda)\lambda^4$ of these two compounds are compared in Figs. 4 and 5. J is only 1,200 for 1 : 2 : 3 : 4-dibenzanthracene, compared with $J = 6{,}200$ for 3 : 4-benzpyrene, showing the major difference in their dipole-dipole resonance with tryptophan.

The values of J and carcinogenicity index for other polycyclic hydrocarbons are listed in Table 1. All the carcinogens have high values of J, with the sole exception of the weak carcinogen 3 : 4-benzphenanthrene, while the non-carcinogens have usually low values of J. Some of the larger non-carcinogenic molecules (for example, pentacene, pentaphene), which have E_1 well below the active region, have anomalously large values of J due to the overlap of their 2nd π-singlet absorption band with the tryptophan emission. If only the overlap with the 1st π-singlet absorption band of the hydrocarbon is considered, and the corresponding overlap integrals J_1 are evaluated, these anomalies disappear. The use of J_1 rather than J appears justified, since the tryptophan emission occurs from the 1st excited π-singlet state which may be expected to resonate with the corresponding excited state of the hydrocarbon. The polarizations of the 1st and 2nd excited states are orthogonal, and it is suggested that the hydrocarbon molecules are bound to the proteins with their axes and planes approximately parallel to those of the tryptophan molecules. Such alignment would greatly enhance the resonance with the 1st excited state, and exclude resonance with the 2nd excited state.

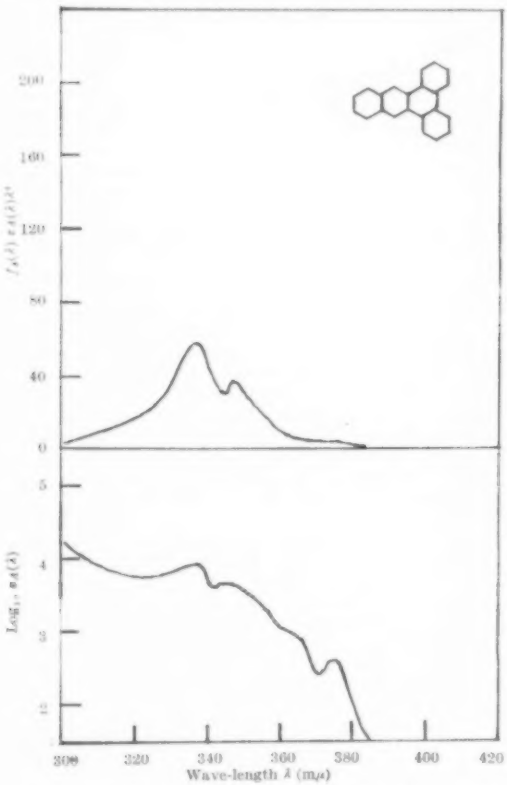

Fig. 4. 1 : 2 : 3 : 4-dibenzanthracene. Absorption ($\log_{10} \varepsilon_A$) and 'tryptophan overlap' ($f_a(\lambda)\ \varepsilon_A(\lambda)\lambda^4$) spectra

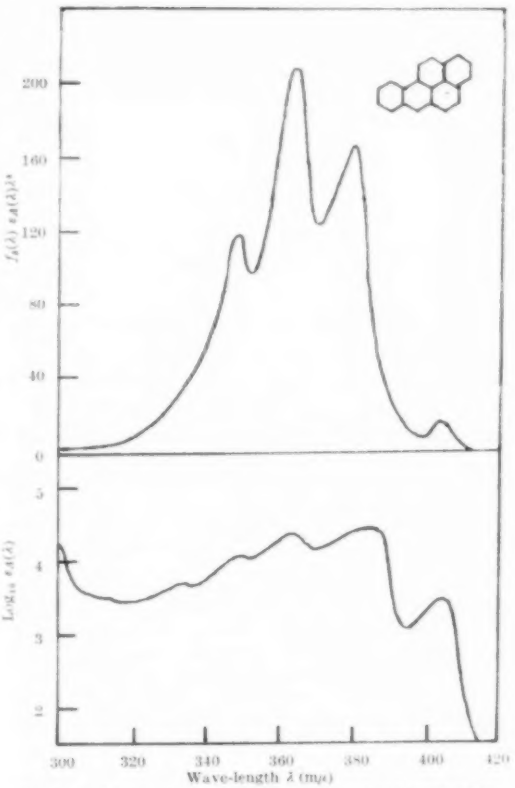

Fig. 5. 3 : 4-benzpyrene. Absorption ($\log_{10} \varepsilon_A$) and 'tryptophan overlap' ($f_a(\lambda)\ \varepsilon_A(\lambda)\lambda^4$) spectra

On the basis of the close correlation observed between J_1 and carcinogenicity, it is proposed that a primary carcinogen should satisfy two fundamental conditions: (1) it should form a bound complex with protein; (2) its first singlet π-electron absorption band should overlap strongly the emission spectrum of tryptophan, yielding a high value of J_1. Neither of these conditions requires that the primary carcinogen should necessarily undergo any chemical

Table 1. Polycyclic Hydrocarbons: Tryptophan Resonance Integrals and Carcinogenicity

	J	J_1	Carcinogenicity
Benzene	0	0	0
Naphthalene	0	0	0
Phenanthrene	0	0	0
1 : 2-benzpyrene	1,750	~200	0
Picene	1,600	~260	0
3 : 4-benzphenanthrene	400	400	+
Chrysene	500	500	0
1 : 2 : 3 : 4-dibenzanthracene	1,200	~1,000	0
1 : 2-benzanthracene	1,350	1,350	?
Anthracene	1,550	1,550	?
1 : 2 : 7 : 8-dibenzanthracene	2,950	~1,900	+
1 : 2 : 5 : 6-dibenzanthracene	3,350	~2,400	+ +
3 : 4 : 8 : 9-dibenzpyrene	3,600	~2,500	+ + + +
1 : 2 : 3 : 4-dibenzpyrene	5,700	~3,300	+ + +
3 : 4-benzpyrene	6,200	~6,000	+ + + +
Pentacene	2,600	0	0
Pentaphene	7,750	~100	0

change, thus distinguishing the present theory from alternative biochemical theories of carcinogenesis. This is consistent with the observations of Peacock, Beck and Anderson[9], who found that 3:4-benzpyrene persisted in its original form in mouse skin tissue over a period of 4 months, during which tumour initiation occurred. They concluded that the chance of inducing a tumour varied directly as the persistence of unchanged benzpyrene at the site of injection.

The proposed theory is consistent with the 'protein-deletion' hypothesis of carcinogenesis, favoured by Haddow[10], which considers that the interaction between carcinogen and protein leads to the loss of function of proteins involved as enzymes essential for the control of growth. The results indicate that the deleted proteins are those containing tryptophan. This is consistent with biochemical observations[11] that mouse tumour tissues are about 20 per cent deficient in tryptophan content compared with normal 'controlled' tissues.

Perhaps the most interesting aspect of the theory is that it indicates that the tryptophan molecules are in their 1st excited π-singlet state at some stage in the normal biochemical process, and that it is the loss of this excitation energy by resonance transfer to the carcinogen which hinders or prevents the protein synthesis.

Note added in proof. Other cellular constituents, notably the DNA and RNA purines, guanine and adenine, also have π-excitation states at ~ 4 eV., and fluoresce weakly at $\lambda \sim 350$ mμ. The postulated π-excitation, which is similar to that observed in bioluminescent systems, where it is produced by oxidation, might therefore be associated with the genetic and biosynthetic processes.

Further studies of complex formation and of energy transfer between molecules of biological interest are being made to elucidate more fully the mechanisms of carcinogenesis and other biological processes.

I wish to acknowledge the assistance of Dr. F. H. Read, who evaluated the overlap integrals.

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NATURE OF THE 'INFECTIVE RIBONUCLEIC ACID COMPONENT' IN CELLS INFECTED WITH ENCEPHALOMYOCARDITIS VIRUS AND THE 'VIROSOME' CONCEPT

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PHENOL extraction at 4° C. of ascites tumour cells infected with murine encephalomyocarditis virus yields infective ribonucleic acid (RNA), although the latter cannot be extracted from the purified virus by similar treatment[1]. Evidence has been presented that the RNA component in infected cells is a virus precursor[2] synthesized in the nuclei[3] during the eclipse phase; it is not deposited with the virus when crude virus preparations are centrifuged[1], but apart from this little is known of its nature. The nature of this component has been investigated by treatment with ribonuclease and papain and reported here.

Infective RNA treated with ribonuclease did not give rise to virus when added to susceptible cells, although untreated RNA did so[1]. Ribonuclease treatment (1 μgm./ml.) of cells infected with RNA greatly reduced the number of cells releasing plaque-forming virus, even when the enzyme treatment was delayed until 2 hr. after infection (Table 1). On the other hand, ribonuclease treatment of cells infected with murine encephalomyocarditis virus did not reduce the number of cells releasing virus if the enzyme were added at 1 hr. or at 4 hr. after infection (Table 1). This suggests that in the RNA component susceptible to phenol extraction and synthesized between 1 hr. and 4 hr. after infection[2], the RNA itself is not 'free', or in any way accessible to the action of ribonuclease.

This suggestion was further supported by experiments in which a series of concentrations of the enzyme was added to cells 1 hr. before infection, and the infected cells then left to synthesize virus while still in contact with the enzyme. Yields of infective RNA and of infective virus after one cycle of virus growth were determined at each enzyme concentration, as was the number of cells killed by virus (Table 2). Ribonuclease did not significantly decrease the amount of virus produced or the number of cells killed; the infectivity of RNA preparations was only affected at enzyme concentrations equal to or greater than 100 μgm./ml. Phenol extraction may not remove all ribonuclease from preparations containing such a high concentration of enzyme, so

Table 1. EFFECT OF RIBONUCLEASE ON CELLS INFECTED WITH RNA OR WITH VIRUS

Cells treated with :	Cells/ml. forming plaques when tested at the stated time after infection 1 hr.	2 hr.	4 hr.
RNA*	$2{\cdot}3 \times 10^3$	$1{\cdot}5 \times 10^3$	—
RNA* then ribonuclease†	$2{\cdot}0 \times 10$	$7{\cdot}0 \times 10$	—
Virus‡	$4{\cdot}8 \times 10^3$	—	$1{\cdot}2 \times 10^4$
Virus‡ then ribonuclease†	$7{\cdot}0 \times 10^3$	—	$9{\cdot}5 \times 10^3$

* Cells 5×10^6/ml.; RNA 5×10^4 plaque-forming units/ml. Number of cells releasing virus calculated as the difference in plaque titre between the whole culture and the supernatant after centrifuging at 500*g* for 5 min.
† Cells incubated with 1 μgm./ml. crystalline ribonuclease for 15 min. at room temperature.
‡ Cells 5×10^6/ml.; virus 5×10^6 plaque-forming units/ml. Number of cells releasing virus estimated by direct plating of cells after antiserum treatment and washing.

Table 2. Effect of Ribonuclease present during Virus Growth

	Ribonuclease concentration (μgm./ml.) 0	0·1	1	10	100	1,000
Virus yield (plaque-forming units/ml. × 10^8)	2·9	5·5	4·2	4·1	7·5	4·0
Cell death (per cent stained by eosin)	78	92	93	71	74	86
RNA infectivity (LD_{50}/ml. × 100)	150	150	100	150	1·5	0·3

Cells (1 × 10^6/ml.) left for 1 hr. at room temperature with ribonuclease, and then infected with 3 plaque-forming units/cell of murine encephalomyocarditis virus. After 5 min. more at room temperature, the cells were diluted in Earle's saline and kept in suspension culture for 17 hr. The concentrations of enzyme were thus reduced after infection to one-fifth of those shown, although the absolute amounts of infected cells and enzyme remained constant.

that at least some of the loss of infectivity may have been caused by residual ribonuclease attacking RNA 'freed' by phenol extraction. However, even if the effect of the enzyme at high concentration is on the RNA component itself, the latter must be at least 100 times more resistant to the action of ribonuclease than 'free' RNA.

These experiments did not exclude the possibility that ribonuclease cannot penetrate the cell or nuclear membrane, so that the RNA component in its intracellular location is protected from enzyme attack. This seems unlikely, however, since ribonuclease can apparently overcome these barriers in cells infected by RNA preparations. Such protection was also excluded experimentally by homogenizing and fractionating cells 3 hr. after infection with virus and then incubating each fraction with 5 μgm./ml. ribonuclease for 30 min. at room temperature. RNA was extracted from the fractions using cold phenol and titrated in mice (Table 3). No significant change in the infectivity of RNA from any fraction could be detected following enzyme treatment.

Table 3. Resistance of Fractions of Infected Cells to Ribonuclease

RNA preparation from :	Infectivity of RNA (LD_{50}/ml.) Untreated control	Ribonuclease treated
Whole cells	501	1,000
Nuclei	39·8	39·4
Mitochondria	42·2	39·8
Microsomes + sap	14·7	28·8

Cells were infected with 4 plaque-forming units/cell of murine encephalomyocarditis virus, incubated for 3 hr. at 37° C., lysed by osmotic shock (Martin, E. M., Coote, J., and Work, T. S., unpublished work), homogenized, and fractionated by centrifugation. A sample of each fraction was incubated with 5 μgm./ml. crystalline ribonuclease for 30 min. at room temperature. RNA was prepared from treated and control samples and tested for infectivity.

The resistance of the RNA component to ribonuclease can be partly overcome by preliminary incubation with a proteolytic enzyme, papain (Table 4). When the 10,000*g* deposit of lysed-infected cells (nuclei and mitochondria, containing most of the RNA component 3 hr. after infection[3]) was exposed to papain concentrations up to 10 μgm./ml., the RNA which could be extracted was not rendered less infective. However, ribonuclease treatment following the papain reduced the infectivity of RNA by one logarithmic unit. RNA extracted from fractions treated with 100 μgm./ml. papain followed by 5 μgm./ml. ribonuclease totally lacked infectivity; but this concentration of papain by itself considerably reduced the amount of infective RNA which could be recovered. Thus it would seem that the RNA component contains a protein which is combined in

Table 4. Effect of Papain and Ribonuclease on the RNA Component

Papain concentration (μgm.)	Infectivity of RNA (LD_{50}/ml.) Untreated control	Treated with ribonuclease
0	4,200	—
1	4,200	68
5	6,800	680
10	4,900	68
100	19	0

Cells were lysed by osmotic shock 3 hr. after infection with 4 plaque-forming units/cell of murine encephalomyocarditis virus. The lysate was centrifuged at 10,000*g* for 15 min. and the deposit was suspended in cysteine–versene citrate buffer *p*H 7·5. Papain was added to give the concentrations shown and the samples were incubated at 37° C. for 30 min. The *p*H was then adjusted to 8·0 and ribonuclease was added to a sample to give a concentration of 5 μgm./ml.; an untreated sample served as a control. After 30 min. at room temperature, the samples were frozen. RNA was extracted and tested for infectivity.

such a way that it is susceptible to the action of papain, but normally protects the RNA from the action of ribonuclease.

The RNA component in cells infected with murine encephalomyocarditis, therefore, probably consists of ribonucleoprotein particles, which represent the 'vegetative' form in which the virus is present during the eclipse phase. These ribonucleoprotein particles are smaller or less dense than the virus[1], or the microsomes of the infected cell, and we propose to call them 'virosomes' by analogy with ribosomes. RNA extracted from virosomes is infective, but since little plaque-forming material can be recovered from infected cells during the time when large numbers of virosomes are present, the particles themselves may have a low probability of initiating infection.

Franklin, Wecker and Henry[4] also showed that ribonuclease treatment (10 μgm./ml.) of a homogenate of mouse brain infected with mouse encephalomyelitis virus did not reduce the infectivity of the RNA afterwards extracted by phenol at 4° C. They concluded that the sole source of infective RNA from infected tissues was the virus particle, based on the fact that infective RNA could be obtained from purified virus using hot phenol and the assumption that only the virus particle is resistant to ribonuclease. Our results, however, suggest that some virus precursors may be resistant to ribonuclease. Moreover, theoretical difficulties occur if their conclusions are extended to other viruses which, like murine encephalomyocarditis, lack a stage sensitive to ribonuclease in multiplication. If RNA becomes infective only after incorporation into mature virus, it should be impossible to extract infective RNA from infected cells before mature virus particles are present. Since there is an increase in the quantity of infective RNA extracted during the first four hours after infection with murine encephalomyocarditis virus, it would, therefore, be necessary to postulate an increase in the number of mature infectious particles present during this time, and one would expect that this increase would be detectable by other means. There is good experimental evidence that a true eclipse phase occurs in the multiplication of murine encephalomyocarditis virus[5] and that the source of infective RNA is not the virus particle[1].

The eclipse phase, infectivity of extracted RNA and ribonuclease resistance of 'vegetative' virus, can be reconciled by the concept of the virosome. The infectivity of virus is then a property of its RNA, but in the infected cell this is present during the eclipse phase in small ribonucleoprotein particles,

virosomes. The function of the virosomal protein is unknown; it may be involved in synthesis of virosomal RNA or simply be required to protect or stabilize the RNA. This protein presumably lacks the specific surface structure, which, in the mature virus particle, is necessary for adsorption or penetration of the cell, while the ribonucleoprotein particle may be too large to be taken up like a molecule of RNA; in this case, the virosome would not be infective and an eclipse phase would be observed. After eclipse, the virosome is coated with surface protein and acquires the properties of the infective particle. This extra protein may also make the particle more resistant to phenol extraction, so that it is necessary to use hot phenol to obtain an equivalent yield of infective RNA.

In the case of viruses with a ribonuclease-sensitive stage in multiplication[6], the RNA in the 'vegetative' state may be either bound or free, since some ribonucleoproteins are sensitive to the action of ribonuclease[7]. If these ribonuclease-sensitive materials were shown by some other means to consist of easily dissociated ribonucleoprotein particles, they too could be called virosomes, providing they contained infective RNA but themselves had a low probability of initiating infection. In the test for infectivity of ribonucleoprotein particles, it would be essential to exclude that due to spontaneously liberated RNA. Therefore, virosomes may not be confined to virus systems without a ribonuclease-sensitive stage in multiplication.

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HÆMOGLOBIN F: ITS SIGNIFICANCE IN THE GENETICS AND EVOLUTION OF HÆMOGLOBIN

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THE recent hypothesis of Ingram and Stretton[1] visualizes the thalassæmias as true hæmoglobinopathies characterized by amino-acid substitutions in either the α- or the β-chain of the hæmoglobin molecule, which remain electrophoretically 'silent' because they do not alter the net electric charge but manifest themselves by depressing the rate of synthesis of hæmoglobin. The theory covers the genetic mechanisms controlling the structure and production of α- and β-chains and thus of the major adult hæmoglobins, but does not specifically account for the γ-chains of fœtal hæmoglobin, for the occurrence of which under normal and pathological conditions no satisfactory genetic hypothesis has yet been offered.

We wish to extend the speculation so as to account for the formation of hæmoglobin F and to present a unifying concept which relates the biochemical and genetic facts concerning hæmoglobin synthesis in the course of normal development as well as in the thalassæmias and the hæmoglobinopathies to basic control by the two pairs of genes known at present as α- and β-genes. Our thesis is that the production of γ-chains is under the control of the same pair of genes which determines the formation of β-chains, once the maturation of the fœtus has reached the point where adult hæmoglobin can be made. We are aware that this concept involves seemingly radical departures from present notions concerning the effects of the genetic coding mechanism on protein synthesis. On the other hand, the hypothesis seems capable of reconciling an extraordinary number of as yet poorly explained observations of diverse nature, clinical, hæmatological, biochemical, genetic and evolutionary, which form a body of evidence no fundamental theory can ignore.

The concept arose from the study of Caucasian pedigrees in which two distinct thalassæmia genes could be identified in heterozygotes by their divergent effects on the minor components hæmoglobins A_2 and F (ref. 2). One gene produced the now familiar pattern of an elevated A_2 fraction[2] with normal or barely elevated values for hæmoglobin F, the other was consistently associated with normal values for A_2 but exceptionally high levels of hæmoglobin F, ranging from 4 to 12 per cent. The presence of the two variant genes in one person had resulted in the classical picture of homozygosity, Cooley's anæmia, that is, the genes 'interacted'.

It is now known that both hæmoglobins A_2 and F possess α-chains[4,5]. The elevation of either component in a thalassæmic heterozygote thus militates against a depression of α-chain formation and indicates that both thalassæmia variants observed by us were of the β-variety, involving substitutions in a β-chain. The difference between hæmoglobins F and A_2 resides in the polypeptides complementary to the α-chains, the former possessing γ-chains whereas the latter has now been shown to contain so-called δ-chains[4]. Since the primary effect of β-genes should be limited to substitution and depression of synthesis of β-chains proper, the question arose how in these β-thalassæmias the variant β-genes could mediate differentially another effect, namely, the elevation of a γ-compound in one case and a δ-compound in the other. Clearly a simple compensatory mechanism involving independent effects of hypothetical γ- or δ-genes was not adequate.

The simplest possible assumption seemed to be that the character or site of the substitution in the β-chain itself determined the nature of the by-product, γ or δ, accumulating in consequence of a 'block' in the metabolic pathway of β-chain synthesis. Depending on the nature of the block caused by one or the other substitution, one or the other alternate pathway was being utilized and the resultant γ- or δ-chains (that

is, potential β-chains which failed to achieve normal structure) combined with available α-chains to form either haemoglobins F or A_2. The two thalassæmia genes might accordingly be written $\beta^{X\gamma}$ (or β^{XF}) and $\beta^{X\delta}$ (or β^{XA_2}) to characterize the two substitutions.

In this view, γ- and δ-chains become primitive or altered β-chains, the production of which would thus be controlled by β-genes. Regarded as primitive β-chains, the γ-chains of the alkali-resistant haemoglobin F of the fœtus should then also be controlled by the genes which in later life determine the production of β-chains. On this hypothesis, the 'switch-over, from haemoglobin *F* to haemoglobin A in the normal fœtus can be viewed as a modulation of a single genetic effect, induced in the course of maturation, an event for which many precedents are known in the behaviour of enzymes and hormones. At a given point in ontogeny a previously inactive enzyme may become active, opening up a new metabolic pathway, and the same gene which earlier induces synthesis of γ-chains now expresses its complete structure and induces β-chain formation.

The implication that γ- and β- (as well as δ-) chains have large parts of their structure in common is in keeping with the results of 'fingerprinting' and amino-acid analyses of human haemoglobins[6]. The further implication that a common pathway is utilized in the synthesis of ultimately divergent products requires the assumption that protein molecules can be assembled in a step-wise manner, a possibility not yet excluded by the known facts concerning the template action of the genic substrate DNA. This assumption is not necessarily in conflict with the basic concept of fixed genetic templates. It merely stipulates that the same complement of genetic material present in the fertilized ovum as in the fully developed individual may exert different effects under different conditions of internal or external environment.

The consequences of this hypothesis as applied to normal and abnormal human haemoglobin synthesis can now be examined.

If γ-chains represent an early and β-chains a later expression of the activity of β-genes, it becomes possible to visualize how the same erythrocytes can contain both haemoglobins F and A. As the final metabolic system matures, β-chains can be made in cells already containing a complement of 'primitive β', that is, γ-chains. Increasingly the production of newly synthesized haemoglobin will entail the use of the ultimate pathway. The gradations observed in the acid-resistant staining of haemoglobin of neonatal erythrocytes[7] correspond to the proportion of γ- and β-chains in each individual cell. The γ-pathway would seem to be a simpler one which always remains open. Synthesis of β-chains is relatively more complex, though once established it is the more efficient mechanism; but a residual minimum of utilization of the γ-pathway always persists, hence the minute amount of haemoglobin F in the normal adult.

It is more difficult to speculate on the biochemical and genetic basis for the production of the δ-chains of haemoglobin A_2. Stated in a general way, our original observations indicate that primary control by β-genes influences the rate of production of δ-chains and possibly the activity of δ-genes if such exist. One might visualize the utilization of a common pathway which would permit the hypothetical δ-genes to complete manufacturing δ-chains only if the sequence of amino-acids up to the 'branching-off point' under the primary control of β-genes were normal, and one might then use the purely operational term, 'secondary genes', for δ-genes. For the purposes of our main hypothesis pertaining to the genetics of haemoglobin F and its evolutionary meaning, it is immaterial whether such a relationship or one of several alternatives is assumed. The crucial point remains the actual observation that certain substitutions in a β-chain appear somehow to regulate the production of both γ- and δ-chains.

The assumption that the formation of γ-chains utilizes a simpler pathway than that of β-chains can be interpreted in terms of evolutionary theory. The alkali-resistant adult haemoglobin of lower animals may be indicative of a γ-chain component reflecting an earlier evolutionary stage, and the final development of a β-chain type of haemoglobin may represent a relatively late achievement of higher species brought about by a mutation of a 'γ-gene' to a 'β-gene'. If this were true, the transient occurrence of a γ-chain type, haemoglobin F, in the human fœtus would be truly part of the recapitulation of phylogeny. An even more speculative possibility is suggested by the ontogenetic stability of the α-chains, which may be a still older evolutionary species of polypeptides utilized for haemoglobin formation. The development of the γ-β type might then represent itself a mutation of an original α-gene, and one is tempted to coin the terms palæo-, meso- and neo-haemoglobins.

As visualized by Ingram and Stretton, the many amino-acid substitutions theoretically possible in either the α- or the β-chain of the haemoglobin molecule allow for many variants of either type of thalassæmia. The substitution may be more drastic than those leading to a mere increase of γ- or δ-residues and may result in the production of identifiably anomalous compounds such as haemoglobin Lepore[8], which appears to be the expression of still another β-thalassæmia gene. It is of interest that in thalassæmic heterozygotes with haemoglobin Lepore, as in the heterozygotes with the $\beta^{X\gamma}$ type of gene observed by us, the A_2 fraction was not increased, suggesting that this particular block likewise could not be associated with increased utilization of the normal δ-pathway. The combination of the Lepore trait with an 'ordinary' thalassæmia gene of type $\beta^{X\delta}$ resulted in thalassæmia major, as might be expected in an individual lacking the genetic mechanism for the production of normal β-chains altogether.

It would appear that in the presence of a severe block in β-chain synthesis, γ-chains are most readily made, presumably because the pathway utilized for their production is always open—as if the block were 'distal' to the 'branching-off point'. Thus, haemoglobin F accumulates in all situations in which there is severe interference with the synthesis of both β-chains, whether the gene combination produces two identical or merely similar substitutions $(\beta^{X\delta})_2$ ('classical' thalassæmia), $(\beta^{X\gamma}\beta^{X\delta})$ (the homozygote observed by us), $(\beta^{X\delta}\beta^{X\,Lepore})$ (Lepore-thalassæmia), and probably in other variants yet to be found. The large concentrations of haemoglobin F in thalassæmic homozygotes as well as the great individual variations reported from case to case (20–90 per cent) become understandable when viewed as the result of blocks of varying severity in the synthesis of β-chains.

The genetic basis for the large amounts of haemoglobin F found in carriers of the so-called 'High F' gene is obviously very different from that involved in thalassæmia. Such persons show no hæmatological

abnormality but exhibit 20–40 per cent hæmoglobin F (ref. 9). The gene is transmitted in a simple Mendelian manner and appears to be allelic to the genes for hæmoglobin S, C (ref. 10) and others already known to represent β-chain mutations[1]. The high percentage of hæmoglobin F presumably reflects not secondary accumulation of γ-chains resulting from a block in the synthesis of an altered β-chain but a 'back mutation' of a β-gene, making it assume the more primitive DNA structure coding for γ-chains as postulated in the evolutionary theory above—a molecular atavism as it were. The existence of such a mutation does, in fact, strengthen the evolutionary hypothesis.

It now seems possible to grade the various substitutions in the β-chain on the basis of the severity of the resultant blocks. Evidently the thalassæmias represent the most drastic of the many possible substitutions, since γ- and/or δ-chains accumulate, at least to a small degree, even in the heterozygous state. Synthesis of hæmoglobin is so severely reduced that the individual erythrocytes cannot fill themselves with pigment and become hypochromic–microcytic. By contrast, the substitutions involved in the sickling mutation and in hæmoglobins C, E, G and F (when produced by the 'high F' gene) are less drastic, that is, they reduce the rate of synthesis of the abnormal β-chains to a lesser degree. No γ- or δ-chain residues accumulate and no hæmatological effects are observed in the simple heterozygous condition. However, the occurrence of target cells in some of these states suggests less-than-optimal filling of the erythrocytes with hæmoglobin, in keeping with the reduced proportion of the abnormal hæmoglobin as compared to hæmoglobin A in heterozygotes; but the reduction in total cellular hæmoglobin synthesis is not great enough to lead to measurable microcytosis. Some substitutions may not appreciably affect the rate of synthesis.

One might thus construct a tentative 'map' of the polypeptide substitutions based on the relative severity of the resultant blocks (and not to be construed in any strict 'geographical' sense) as follows: $\beta^{A}\gamma \rightarrow \beta^{A}$ *Lepore* $\rightarrow \beta^{A}\delta \rightarrow \beta^{S}$, β^{E} and $\beta^{C} \rightarrow \beta^{D}$, β^{F} and $\beta^{G} \rightarrow \beta^{A}$.

Homozygosity should result in increased production of hæmoglobin F in proportion to the severity of the resultant block. The thalassæmias, representing the most drastic substitutions, show the highest proportion of hæmoglobin F. Thalassæmia major is also the severest of the clinical syndromes, with severe anæmia and hæmoglobin deficit within the red cells.

Homozygosity for the sickling gene is complicated by the catastrophic effects which the physical state of hæmoglobin S in deoxygenated cells can produce on the survival of erythrocytes. Here the additional stress created by the rapid rate of hæmolysis may enhance the effect of a mutation which, in terms of its primary effect on the rate of hæmoglobin synthesis, would appear to be relatively mild, judged from the heterozygous state. Thus the demands made on enzymatic processes for the synthesis of the abnormal β-chains may be inordinately great, and part of the available substrate is forced into the less demanding γ-pathway. This may explain the presence of variable and usually modest amounts of hæmoglobin F in homozygotes for the *S*-gene, and the absence of hæmoglobin F increases in homozygotes for the *C*-gene, which causes a substitution at exactly the same point in the molecule.

When a β-thalassæmia gene is combined with another β-chain mutant such as *S*, *C* or *E*, the affected individual is unable to make any normal β-chains. In such double heterozygotes, hæmoglobin F may be expected to accumulate to an extent determined by the nature of the substitutions. The interaction effect apparent in the high proportion of the abnormal hæmoglobin S, C or E in persons who possess only one gene for S, C or E reflects the fact that the thalassæmic substitution is much more drastic than any of the other mutations; or, in other words, that the rate of synthesis of the thalassæmic β-chain is much more depressed than that of the β-chain carrying an S, C or E substitution. The relatively large increases in hæmoglobin F observed in all these interaction syndromes may thus be attributed chiefly to the drastic depression of that β-chain which carries the thalassæmic substitution and is channelled principally if not exclusively into the γ-pathway.

Combinations of two mutant β-genes other than thalassæmia and causing less severe substitution effects might be expected to result in smaller, if any, increases in hæmoglobin F and in less severe anæmias. Sickle cell–hæmoglobin C disease may serve as an example. No increases in hæmoglobin F seem to have been reported. The approximately equal proportions of hæmoglobin S and hæmoglobin C in this condition indicate the equivalence of the substitution effects caused by the *S* and *C* genes (as might perhaps be expected from the similarity of the mutations themselves).

In α-thalassæmias the production of hæmoglobin F—or for that matter of hæmoglobin A_2—should not be enhanced, since these compounds contain α-chains. In non-interacting combinations with sickling or hæmoglobin C genes, α-thalassæmia genes seem to be involved. The proportion of hæmoglobin S or C in such cases is no greater than expected in simple heterozygotes, the inheritance is non-allelic, the proportion of hæmoglobin F is not increased and the values for both hæmoglobin F and hæmoglobin A_2 in the thalassæmic relatives are low or at most normal[11]. Available space does not permit a discussion of the implications of our hypothesis for the group of α-thalassæmias. It may be pointed out, however, that the transient appearance of Bart's hæmoglobin, a γ-tetramere[12], followed by the appearance of hæmoglobin H, a β-tetramere[13], in H-thalassæmia, which has been designated on other grounds as an α-thalassæmia[14], is in keeping with the assumption that the same genes successively induce synthesis of γ- and β-chains.

Small elevations of hæmoglobin F have been observed in a variety of unrelated hæmatological conditions. In the light of the hypothesis presented, this phenomenon may be interpreted as the result of stress leading to maximal utilization of enzyme systems required for β-chain synthesis, with ultimate development of a deficit necessitating the increased use of the alternate (γ) pathway. Such a mechanism was invoked above in order to account for the relatively high concentrations of hæmoglobin F in sickling homozygotes as compared to homozygotes for hæmoglobin C or E genes.

The hypothesis presented here, though based on apparently crucial observations, extends speculatively to many assumptions. It is presented because it seems to fit most observations concerning the structure and genetics of human hæmoglobins and because it can be tested in a variety of ways, experimental and clinical.

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COMPLEMENT-FIXING BLOOD GROUP ANTIBODIES WITH SPECIAL REFERENCE TO THE NATURE OF ANTI-*Le*^{a}

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CERTAIN blood group antibodies are complement fixing, that is, they unite with homologous red cells, complement is fixed and lysis may ensue. In many instances, however, lysis does not result but the aggregate gives a positive antiglobulin test; it is only when the antibody is in high concentration that lysis occurs.

Dacie *et al.*[1] showed that the antiglobulin reagent united not with the antibody but with absorbed complement. In this article *E* represents erythrocytes, *A* antibody, and *C′* complement. In the combination *EAC′*, therefore, antiglobin serum unites with *C′*. Later, Mollison[2] showed that *EA*, although not lysed by human complement, were lysed by certain animal complements, for example, guinea pig, rabbit.

Blood group antibodies that are complement fixing are cold incomplete anti-*H*, anti-Lewis (anti-*Le*^{a} and anti-*Le*^{b}), anti-*Jk*^{a} and anti-*Jk*^{b}, some examples of anti-*Fy*^{a} and anti-*K*, and certain antibodies from cases of cold acquired hæmolytic anæmia; these latter have been studied[3,4] and found to be γ_1-globulins. Although cold incomplete anti-*H* is undoubtedly the commonest antibody, unfortunately, as Dacie[5] originally showed, it does not unite with the red cells in the absence of complement and it is impossible, therefore, to prepare *EA* alone. One of the most useful antibodies to work with is anti-*Le*^{a} and *Le*(*a*+) erythrocytes, particularly since anti-*Le*^{a} is a fairly common antibody. The work described in this article was done using this system.

Stratton[6] showed that *EA* could be prepared using this system, and originally it was found that the sensitized *EA* gave a negative antiglobulin test. It was the combination *EAC′* which, as previously described, gave a positive antiglobulin test. It was also possible to prepare an eluate from *EA* which would unite with *Le*(*a*+) cells producing more *EA*; these *EA* may not themselves give a positive antiglobulin test but would, nevertheless, react with *C′*, forming *EAC′*. Antibody could not be eluted from *EAC′*.

The components of *C′* which are fixed when *C′* reacts with *EA* are shown in Table 1. *C′*2 is completely fixed; this, however, gives no clue as to the nature of the *C′* component on *EAC′* which unites with the antiglobulin serum. This problem was tackled by three groups of workers in somewhat different ways[7–9], but they all came to the same conclusion—the important component was *C′*4.

Table 1. Fixation of *C′* components by *EA*

	*C′*1 (per cent)	*C′*2 (per cent)	*C′*4 (per cent)
Normal serum	100	100	100
Absorbed with normal cells (*E*)	93	80	80
Absorbed with *EA*	73	0	48

Jenkins *et al.*[9] demonstrated that the active fraction of the antiglobulin serum was anti-β_1.

This is a valuable system for studying the action of complement on the sensitized cell *EA*, since in addition to lysis a new sensitive method is available for detecting the absorption of *C′* by *EA*, namely, the antiglobulin test. *Le*^{a} group specific polysaccharide (provided by Prof. W. T. J. Morgan) can be utilized in experiments on sensitized cells. *Le*^{a} substance when mixed with *EA* in a suitable concentration will prevent the treated *EA* fixing *C′*; but it has no effect on the reaction between *EAC′* and antiglobulin serum. Thus, among other things, is another means of determining *C′* fixation[10]. In this system the binding power of complement on the antigen–antibody combination can be demonstrated.

As a preliminary to further investigations on the effect of *C′* on antibody in *EA* it was decided to try to determine the nature of the antibody. Fudenberg, Kunkel and Franklin[11], in a study of high molecular weight antibodies, pointed out that 5–10 per cent of the total γ-globulin of normal serum consists of faster-moving 19*S* component of molecular weight about a million. The other 90–95 per cent consists of 7*S* of a molecular weight of 150,000. It is known that mobility and weight are not necessarily associated, but, for convenience, in this article the two groups are referred to as γ_1- and γ_2-globulins. These workers found certain antibodies belonged to the first, or γ_1-group, for example, often complete antibodies or agglutinins, and others, such as incomplete *Rh* antibodies, to the second group. The main difficulty in this work is that most anti-*Le*^{a} *C′* fixing antibodies are of low activity and the amount of serum protein present as antibody is probably very small indeed. Many of the normal physical methods applicable to their study cannot be used and indirect methods have been employed from which tentative conclusions are drawn.

Work involving electrophoresis of anti-*Le*^{a} antiserum on polyvinyl particle blocks[12] showed that antibody activity was present in the γ-globulin fraction of the serum. The euglobulin fraction of

the serum (prepared at pH 6·4) in certain instances contained all the antibody activity. It was thought possible, therefore, that the antibody belonged to the γ_1-globulin group. Deutsch and Morton[13] showed that sulphydryl compounds, such as mercaptoethanol, dissociate macroglobulins, and Grubb[14] applied this to study the effect of this treatment on sera containing blood group antibodies. Using essentially similar methods anti-Le^a sera so treated would not make *EA* or *EAC'* when mixed with $Le(a+)$ erythrocytes, even after the addition of *C'*. This is what would have been expected if the antibodies were heavy-weight γ-globulins.

Many different anti-Le^a antisera were used to prepare *EA*. All the examples of *EA* originally prepared were un-agglutinated by routine or commercial antiglobulin sera, or even by those prepared following immunization of rabbits with euglobulin fractions of normal human serum. Nevertheless, that such an antiglobulin serum was united with *EA* was suggested by its ability to impair or abolish human *C'* fixation by *EA* pre-treated with antiglobulin serum. Afterwards, potent anti-Le^a sera were found from which *EA* could be prepared which were agglutinated by anti-euglobulin antisera (Table 2).

Experiments were done involving the titration of sensitized cells *EA* with antiglobulin sera, together with tests of the inhibiting effect of γ_1- and γ_2-globulin preparations on the ability of anti-γ_1 serum to agglutinate sensitized cells. Prof. N. Martin provided anti-γ_1 and γ_1-globulin, and the γ_2-globulin preparation used was free from heavy component. *EA* were prepared using several different anti-Le^a, and the *Rh* sensitized cells were coated with antibody considered to be a γ_2-globulin (Tables 2 and 3). Additional tests[12] also showed that α- and β_1-globulins were non-inhibitory. Table 4 shows that there is a correlation between the titre of the antiglobulin serum with the *EA* and the extent of their lysis by absorbed guinea pig serum. This suggests that the differences of antiglobulin titre may be due to differing amounts of antibody on the *EA*. These results (Tables 2, 3 and 4) suggest that the antibody on *EA* is a γ_1-globulin.

Further experiments on the effect of Le^a substance and mercaptoethanol on the sensitized erythrocytes, *EA* themselves, provided additional information. If a 10 per cent suspension of *EA* (iii, Table 2) was mixed with an equal volume of 2×10^{-3} solution of Le^a substance at 37° C., the *EA* were not then agglutinated by the antiglobulin serum. Secondly, treatment of *EA* with 0·2 *M* mercaptoethanol at room temperature for 2 hr. resulted in a negative antiglobulin test and the titration score[15] fell from 15 to 0, but if *Rh*-sensitized cells were similarly treated the titration score was reduced only from 26 to 23. The mechanism of these effects is not entirely clear, but it does suggest that normally the antiglobulin serum is united with the absorbed antibody. This is important because it is possible that serum proteins, other than antibody, may be absorbed on to *EA* at the time of their preparation (cf. Vaughan[16]). The second group of experiments will be more fully described elsewhere.

In reaching the conclusion that these *C'* fixing anti-Le^a antibodies are heavy-weight γ-globulins, it must be borne in mind that the γ_1-globulins used in inhibition tests and for the preparation of antibodies are from cases of macroglobulinæmia and, therefore, are pathological and not normal serum proteins.

Table 2. Titre of Antiglobulin Sera with Various Sensitized Cells*

Test cells*	Antiglobulin titre: Anti-euglobulin	Anti-γ_1
EA i	0	16
ii	1	16
iii	8	128
iv	16	512
Rh-sensitized cells	64	1,024

* *EA* prepared with different anti-Le^a i–iv.

Table 3. Inhibition Tests

A Substances added to equal vol. of anti-γ_1 dil. 1/20	*B* Antiglobulin test mixtures from column *A*: *EA* (iv)*	*Rh*-sens.*
Saline	+ + + + +	+ + + + +
γ_1-Globulin dil. 1/400	Neg.	+ + + + +
γ_2-Globulin dil. 1/25,000	+ + + + +	Neg.
γ_2-Globulin dil. 1/1,000	+ + + +	Neg.
γ_2-Globulin dil. 1/100	Neg.	Neg.

* As in Table 2.

Table 4. Relationship between Antiglobulin Titre and Lysis of *EA*

Test cells*	Antiglobulin test titre	Lysis with absorbed guinea pig serum (per cent)
EA i	0	0
ii	2	0
iii	8	40
iv	16	70
E	0	0

* As in Table 2.

Practical applications of these observations spring to mind. An antibody, anti-γ_1, active against the antibody is available, together with another, anti-β_1 (ref. 9), against absorbed complement; these facilitate the study of the action of *C'* on *EA* (ref. 10). Wiener *et al.*[17] have used a system involving the neutralization of antiglobulin serum for the detection of human serum globulins. The results shown in Table 3 may be taken to illustrate the known cross-reactions between γ_1- and γ_2-globulins or their impurity. Purified protein preparations prepared by chemical methods must always be regarded as impure when considered for immunological work and, similarly, an antibody prepared in animals is not merely an antibody against a single protein but also contains a spectrum of antibodies. Thus far, the system has been used only for the assessment of the relative purity of serum fractions supposedly predominantly either γ_1- or γ_2-globulin.

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EFFECTS OF IONIZING RADIATIONS ON RICE PLANTS

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THE effects of ionizing radiations on various plants have been reported by many investigators since the early work of Stadler[1,2]. Hence, there exists a wealth of information on the radiophytological responses. The results of plant reactions during the first year of study on radiation induction of useful mutations in a rice crop are presented here and discussed with the view of enlarging our present knowledge of radiobiological effects.

Five varieties of Burmese rice (*Oryza sativa* var. *indica*)—*A*36–3, *B*401, *C*28–16, *D*25–4 and *Xq*–4—were each irradiated both with 25 kr. and 35 kr. of X-rays at the Brookhaven National Laboratory, after exposure to a relative humidity of approximately 60 per cent for about 2 weeks. Nearly 3 weeks after this processing, some of the irradiated seeds were germinated here on moist filter-papers in Petri dishes on May 11, that is, about one month in advance of normal sowing season which usually falls due in mid-June. The remaining lot set aside at room temperature was likewise sprouted on June 15 to study the storage effect, if any.

The sprouts were transferred from dishes to earthen pots during 3–6 days following germination. Water was supplied regularly and close observations were made daily. All were uprooted, measured, photographed, and transplanted in pots when about 32 days old. Seedling fatality was expressed as the number of dead seedlings (per cent of germinants).

Tillerings and heights of transplants were recorded weekly. About 2 weeks before floral emergence, both treated and untreated transplants were properly isolated in linen bags in case of cross-pollination in the irradiated (*R*1) generation. This preventive measure was necessary to ensure that mutants to be screened in generation *R*2 were due to radiation only. Seed fertility was determined by counting the total number of both filled and unfilled grains in each treatment, and then calculating the number of filled grains per hundred of that total number. The susceptibility value of rice plants to false smut disease due to *Ustilaginoidea virens* (Cke.) Tak. was computed as the number of infected grains as a percentage of all filled grains in the treatment.

Four other varieties of Burmese rice—*A*28–81, *B*24–92, *C*33–18 and *D*17–88—after bombardment with thermal neutron fluxes of $6{\cdot}92 \times 10^{9}$/cm.^{2}/sec. and $6{\cdot}70 \times 10^{9}$/cm.^{2}/sec. for 15 and 20 hr., respectively, on July 13 at Brookhaven were germinated, as described, on August 12. Transplantation was completed on September 14, and transplants in the neutron-treated (*N*1) generation were also isolated.

As shown in Table 1, there was practically no difference in germination of rice grains either among varieties or treatments with X-rays or thermal neutrons. On the other hand, Mashima and Kawai[3] reported a decrease in germination-rate of rice grains as a result of exposure to both X-rays and thermal neutrons. Development of sprouting seeds apparently slowed down directly the X-ray dosages increased. During the initial stages of growth in the nurseries, *R*1 seedlings looked like lean, medium-dwarfs with relatively thick, narrow, and dark green leaves, displaying varying degrees of foliar convolution and restricted growth. Only one albina-type mutant showed up among sixty-three 25-kr. members of *B*401, but it did not survive transplantation. Other such chlorophyll-defective mutants as those with chlorotic/yellowish stripes along margins or mid-ribs of leaves were seen on two *C*28–16, two *D*25–4, and one *Xq*–4 members of the 25-kr. treatment.

Fatality and retardation in height of 32-day old rice seedlings generally increased as the X-ray dosages increased (Table 1). Some differences of intervarietal responses were also apparent. Matsuo *et al.*[4] made similar observations on mortality and inhibition of seedling height. However, *B*401 seedlings were taller at a higher dose-rate than at the lower dose-rate. Such an apparent stimulation at a higher dose-rate, and a direct relationship between chronic gamma-ray dosage and degree of growth inhibition in *Vicia faba* were also reported by Sparrow and Gunkel[5]. Ouang and Chang[6] recorded about 10 per cent increase over the control in height of *X*1 (*R*1) plants. A departure from direct proportionality between reduction in height of maize seedling and radiation doses at certain dosages of X-rays or thermal neutrons had been demonstrated by Schwartz[7], though. Moutschen[8] noted the same with barley coleoptiles, the develop-

Table 1. RICE GRAIN GERMINATION, SEEDLING FATALITY, SEEDLING HEIGHT, AND RANGE OF SEEDLING HEIGHTS IN *R*1 AND *N*1 GENERATIONS RAISED ON MAY 11, 1959

Variety	Dosage	Average germination (per cent)	Average fatality (per cent)	Average seedling height (cm.)	Range of seedling height (cm.)
*A*36–3	0 hr. (control)	100	4	59·59	41·3–71
	25 kr.	98	14·2	37·80	21 –57·5
	35 kr.	97	76·3	27·47	8·8–42·4
*B*401	0 hr.	98	5·1	56·77	30 –69·5
	25 kr.	100	37	30·21	16 –46·5
	35 kr.	99	93	37·61	27·9–46·3
*C*28–16	0 hr.	99	3	39·70	25 –52
	25 kr.	98	10·2	25·70	18 –40·5
	35 kr.	98	74·5	20·80	10 –47
*D*25–4	0 hr.	97	5·2	48·98	28 –69
	25 kr.	95	33·6	27·89	19 –56·5
	35 kr.	97	93	23·80	11 –43
Xq–4	0 hr.	100	3	49·46	30·6–68·4
	25 kr.	100	22	29·16	12·7–39
	35 kr.	97	70·1	23·56	9·4–39·1
*A*28–81	0 hr. (control)	96·5	—	43·36	41 –46
	15 hr.	97·5	—	38·14	32 –46
	20 hr.	98	—	37·72	34 –40
*B*24–92	0 hr.	99	—	44·62	42 –46
	15 hr.	98	—	41·85	40 –47
	20 hr.	98·5	—	45·2	40 –50
*C*33–18	0 hr.	95	—	37·94	34 –44
	15 hr.	97	—	36·4	33 –40
	20 hr.	97	—	37·12	33 –42
*D*17–88	0 hr.	94·5	—	41	37 –45
	15 hr.	90	—	40·44	35 –45
	20 hr.	94·5	—	41·56	36 –48

kr., kiloroentgens of X-rays; hr., hours of exposure to thermal neutrons

ment of which depends on both cell-division and cell-elongation. According to Schwartz and Bay[9], seedling growth is determined simultaneously by mitotic inhibition and intensity of chromosomal damage.

As observed by Ehrenberg and Nybom[10] and Caldecott[11] in barley, and Matsuo *et al.*[4] and Yamaguchi[12] in rice, both wide and narrow ranges of seedling heights were obtained; this suggested larger and smaller deviations around mean values in the X-ray and thermal neutron treatments (Table 1), respectively. Contrary to the results of Matsuo *et al.*[4] and Huang[13] on the progressive inhibition of seedling height consequent on increasing bombardment with thermal neutrons, Table 1 indicates no appreciable disparity in height among the treatments.

Table 2 suggests that about one-month delay in sowing clearly enhanced the fatality of seedlings from grains irradiated with X-rays, but did not apparently affect germination of almost all strains tested. The storage effect, as it is termed, was also exhibited in barley seeds, and depended on a number of factors (Caldecott[14]).

Differences in height among treatments may persist in transplants of certain varieties for some weeks. Later these may narrow down close enough to suggest a recovery from the setback in growth at the early stages. Success in attaining the height of the control at the time of flowering of *R*1 wheat plants was also observed by Bora[15]. The stunting effects of X-rays are probably due to gene mutation[6].

Tillering in some strains may vary directly or inversely with the X-ray doses. Yet, most of the tillers in the treated plants were either late or poorly developed and unproductive. The early differences in the numbers of tillers between treatments tended to drop and the number became nearly equal to the control later in the season owing mainly to the death of underdeveloped tillers in certain strains. Natarajan *et al.*[16] and Bora[15] obtained a decrease as well as an increase in the number of tillers in wheat plants, respectively, whereas Ouang and Chang[6] reported both inhibitory and stimulatory effects of X-rays on tillering in rice plants.

Table 3 summarizes the number of panicles per plant, grains per panicle, and percentages of grain fertility and susceptibility to false smut disease, and dates of heading. There was a significant gain in the number of panicles per plant at 35-kr. dose-rate as compared to controls; the exceptions are probably irresponsive *B*401, highly responsive *C*28–16, and adversely affected *Xq*–4 at both levels of X-rays, while such a difference between controls and 25-kr.

Table 2. Rice Seed Germination and Seedling Fatality in *R*1 Generation raised on June 15, 1959

Variety	Dosage	Germination (per cent)	Fatality
*A*36–3	0 hr.	98·8	—
	25 kr.	99·1	37·5
	35 kr.	98·9	82
*B*401	0 hr.	97·9	—
	25 kr.	97·3	95·6
	35 kr.	98·8	100
*C*28–16	0 hr.	99·5	—
	25 kr.	98·47	16
	35 kr.	94·99	100
*D*25–4	0 hr.	93	—
	25 kr.	89	41·5
	35 kr.	85	100
Xq–4	0 hr.	99·1	—
	25 kr.	99·1	39
	35 kr.	95·9	87·1

—, data not taken

Table 3. Number of Panicles and Grains, Percentages of Grain Fertility and Susceptibility to False Smut, and Date of Heading

Variety	Dosage	Average No. of panicles per plant	Average No. of grains per panicle	Average grain fertility (per cent)	False smut susceptibility (per cent)	Date of heading (days)
*A*36–3	0 hr.	13	140	55	0	—
	25 kr.	13	116	8	0·1	†4
	35 kr.	16	111	3	0	—
*B*401	0 hr.	18	119	56	0	—
	25 kr.	18	111	6	0·001	†2
	35 kr.	17	116	16	0	—
*C*28–16	0 hr.	10	180	65	0	—
	25 kr.	14	115	5	0·11	†3–4
	35 kr.	13	124	13	0	—
*D*25–14	0 hr.	17	150	45	0·3	—
	25 kr.	16	136	5	0	†0–1
	35 kr.	20	119	1	0	—
Xq–4	0 hr.	13	164	51	0·06	—
	25 kr.	9	120	11	0·09	†3–5
	35 kr.	9	115	10	0·09	—
*A*28–81	0 hr.	8	97	6	—	—
	15 hr.	9	100	3	—	—
	20 hr.	7	100	3	—	—
*B*24–92	0 hr.	13	103	5	—	—
	15 hr.	8	100	< 1	—	—
	20 hr.	7	99	< 1	—	—
*C*33–18	0 hr.	6	92	15	—	—
	15 hr.	6	98	< 1	—	—
	20 hr.	5	99	< 1	—	—

†, later than control; kr., kilorentgens of X-ray; hr., hours of exposure to thermal neutrons; 0 hr., control; —, data not taken

treatments was mostly lacking; but nevertheless, the panicles of *R*1 plants usually had less grains than those of their respective controls. Essentially, no considerable divergence in grain or panicle numbers was apparent among the thermal neutron treatments. Grain fertility was greatly reduced though not always in progression with the dosages administered. Ouang and Chang[6] and Matsuo[4], however, found a direct relation between the grain sterility and the dosages. As reported[13], the depression of grain fertility seemed to be more severe in thermal neutron than in X-ray treatments. Grain sterility is attributed to chromosomal damage or rearrangement[17,18]. The resistance to false smut disease of all varieties studied remained almost unimpaired at the levels of X-rays used. Most of the *R*1 plants of 25-kr. series came to heading 2–5 days later than the controls. Ouang and Chang[6] noticed earliness as well as lateness in heading of treated rice plants while Huang[13] reported a distinct delay in flowering.

Thanks are due to Dr. H. J. Curtis, Dr. S. Shapiro and Dr. H. H. Smith.

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LETTERS TO THE EDITORS

GEOPHYSICS

Origin of Stone and Iron Meteorites

THE question arises whether meteorites in general have had a common origin, and in particular whether the stone meteorites have had an origin different from that of the iron meteorites. One line of experimentation bearing on this problem is the determination of cosmic-ray exposure ages of meteorites. If the total content of a stable cosmogenic nuclide is measured, and if its rate of production can be determined, then the length of exposure to the radiation is known.

But the rate of production of a stable nuclide must be estimated either from purely theoretical considerations or from measurements on a radioactive nuclide. The theoretical arguments are probably not too reliable at this stage, and the best estimates seem to be based on radioactivity measurements. For example, the tritium decay-rate at the meteorite's time of fall gives directly the tritium production-rate, and if the cross-section ratio $\sigma_t/\sigma_{^3He}$ is known, the helium-3 production-rate can be calculated. Then from measured amounts of helium-3 an age can be determined.

A table of such meteorite ages has recently been compiled by Urey[1]. The helium-3 measurements were carried out by a number of investigators, using either mass spectrometry or activation analysis. The production-rate was calculated on the basis of five tritium measurements in different stone meteorites. Since all the values were approximately equal, it was concluded that the helium-3 production-rate is invariant and equal to 10^{-8} stand. c.c./gm./million years. The production in iron meteorites was chosen as half this value.

These calculations lead to a general trend of ages, as shown in Fig. 1. A discrepancy can be seen to exist between the ages of the stone meteorites and those of the iron meteorites. On this basis it was suggested[1] that the stones and the irons may have had a different origin and history. The irons presumably coming from the asteroidal belt, perhaps the stones come from the surface of the Moon. This would be in line with shorter exposure ages for the stones.

But several refinements which should be made to such an estimation of exposure ages lead to perhaps not negligible adjustments. In particular, one should try to estimate better the difference in helium production-rates in iron and stone meteorites, the dependence on depth of helium production, and

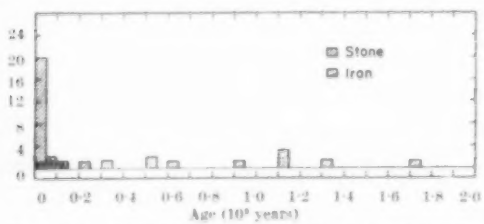

Fig. 1. Cosmic-ray exposure ages of stone and iron meteorites, from the data compiled by Urey (ref. 1)

the effect of space erosion. Some preliminary experimentation has been done on at least the first two of these effects.

Aluminium may be considered to be an element of Z nearly equal to the average for stone meteorites, and $\sigma_{^3He}$ for an iron target has been found to be greater than for an aluminium target[2], increasing to a factor of three at bombarding energies of several BeV. (Schaeffer, O. A., and Fisher, D. E., unpublished results). When one applies this correction to Urey's data, and when data on seven other iron meteorites that have been recently measured[2] are included, the discrepancy in ages between the stones and the irons is largely removed. However, more cross-section data are needed for those elements which actually make up the bulk of stone meteorites.

It is not clear whether the dependence on depth of nuclide production will be important in stone meteorites, although in irons it has been shown[4] that a production-rate taking this factor into account may vary by up to an order of magnitude from estimations ignoring the effect. Eberhardt and Hess[5] assume that the effect will be negligible in stones, because of their rather small size. But many of the stones are of size comparable to several irons in which a serious depth effect has been estimated. Further, Opik has pointed out that stone meteorites have a high probability of shattering on contact with the Earth's atmosphere, so that small fragments found on the Earth may actually have been in a large meteorite in space[6]. If a depth-effect exists, one would expect to find differences in content of both stable and radioactive nuclides within the same meteorite, and differences in content of radioactive nuclides in different meteorites, such as are found in irons. Begemann *et al.*[7] found the same tritium content in two pieces of Norton County stone meteorite, but Fireman and DeFelice[8] found a value half as much in still another piece. Fireman and DeFelice also measured the argon-39 in two pieces of Norton County and found a 30 per cent variation. Eberhardt and Hess[5] measured the helium-3 in four stone meteorites that have been investigated by other workers, and in three of them obtained significantly different values, two of them differing by greater than a factor of ten. Some recent tritium measurements in different stone meteorites suggest a range of values[9]. The argon-39 contents of two stone meteorites were measured[9] and a factor of four difference was found. From these considerations, then, it would appear that a serious dependence on depth may exist in stones.

A scheme for estimating the depth-dependent production-rate of stable nuclides in iron meteorites, based on argon-39, chlorine-36, and rare gas ratio measurements, has been presented[3,4]. It is not so easy, however, to estimate this effect in individual stone meteorites. The rare gas ratios are not expected to vary uniformly with depth, due to radiogenic helium-4 and to a varying chemical composition which will affect neon and argon production. Approximations to the upper and lower limit of helium-3 production-rates in stones can be estimated,

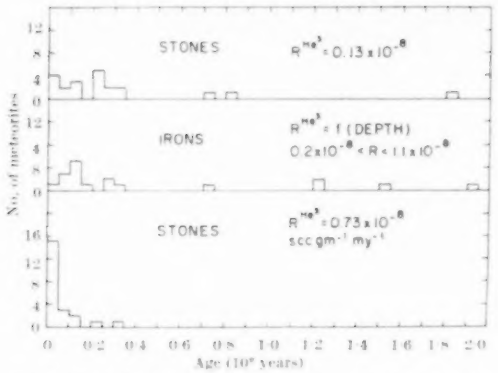

Fig. 2. Depth-dependent cosmic ray exposure ages for stone and iron meteorites. R^{3He} = helium-3 production-rate in standard c.c./gm. of meteorite per million years

however, from the upper and lower limits in the iron meteorites[4] and from the relative cross-sections in iron and aluminium targets. The ages thus calculated are shown in Fig. 2. In this figure ages have been calculated only for those iron meteorites for which all the rare gases have been determined. A production-rate in stones of $0{\cdot}7 \times 10^{-6}$ stand. c.c./gm./m.y. may be compared to that of $1{\cdot}0 \times 10^{-6}$ obtained by Urey on the basis of tritium measurements. Ages have also been calculated[3] for the irons on the basis of their neon-21 and argon-38 contents, and on measured values for the ratios $\sigma_{^3He}/\sigma_{^{21}Ne}$ and $\sigma_{^3He}/\sigma_{^{38}Ar}$ in iron targets. These ages agree well with the helium-3 ages.

The age distribution for the stone meteorites, with $R^{3He} = 0{\cdot}7 \times 10^{-6}$ peak at a lower value than does the iron age distribution. There are several stones with ages of approximately 10–20 million years, and none older than 400 million years, whereas some irons are older than a billion years. However, when R^{3He} reaches $0{\cdot}13 \times 10^{-6}$ in stones, the stone age distribution is no longer different from the iron's. As the depth effect becomes more important in stones, then, their age distribution shifts more towards that of the irons. It should also be noted that a slightly younger age for the stone meteorites is reconcilable with a longer mean life against collision destruction in the asteroidal belt for irons than for stones. From Fig. 2 it does not seem possible to say that there is an age difference greater than can be accounted for by this consideration.

Only a very general statement can be made at this time on the effect of space erosion. However, it should be expected that the combined wearing effect of dust, gas, ions, and electrons in interplanetary space might be quite different for irons than for stones. Fireman and DeFelice[8] have shown that the effect may be quite large, and may be more than two orders of magnitude greater for the softer stones than for irons. This would lead to a shorter apparent age for the stones.

Until more information is forthcoming, then, on more direct radioactive-stable nuclide determinations (such as argon-38/argon-39, as well as hydrogen-3/helium-3), one is not justified in postulating separate origins for the stone and iron meteorites on the basis of their cosmic-ray exposure ages.

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Enhancement of Night-Sky Molecular Nitrogen Emission in Polar Cap Absorption Events

It has long been accepted that auroral activity is associated with magnetic disturbances. Observations inside the auroral zone show the relationship to be rather complex; bright auroral displays are often observed during quiet magnetic conditions, and even in the greatest of magnetic storms visual auroræ are not always observed. On the other hand, well-exposed auroral spectra are always obtained during these storms. The source of this emission lies in extensive glows, often above the threshold of vision, but of such low contrast that observers normally do not recognize or report them. Changes in the colour of the night sky can be observed on colour film exposed during such storms. The forbidden atomic oxygen lines and the first negative, first positive and second positive bands of molecular nitrogen are all enhanced in these glows.

Since the beginning of the International Geophysical Year, patrol spectrographs have monitored the night sky emissions in the Antarctic and Arctic. The zenith intensity of the first negative band of ionized molecular nitrogen at 3914 Å. has been determined during some of the major magnetic storms, at stations situated inside the auroral zone.

The relative intensity of the band at 3914 Å. is plotted on a logarithmic scale in Fig. 1. Curve 1*a* is the intensity variation during May 1959, at South Pole Station, Antarctica, and curve 1*b* is the intensity variation during November 1960, at Thule, Greenland. On May 10, 1959, a flare on the Sun was followed about 6 hr. later by the start of a polar cap absorption event. Soon after the polar cap absorption began, the intensity at 3914 Å. began to increase steadily, reaching a maximum, some 100 times above normal minimum night-time levels, about 24 hr. later, coincident with the peak of activity of the associated major magnetic storm. The intensity then fell steadily, returning to its normal night-time minimum values some 48 hr. after the peak.

In November 1960, two similar events occurred following flares on the Sun, and the sequence of events at Thule is almost identical to the behaviour observed at South Pole Station in 1959. The times of the flares, polar cap absorption commencements and the sudden commencements of the magnetic storms are shown in Fig. 1.

The intensity of the first and second positive bands of molecular nitrogen show the same behaviour as the first negative bands.

In the three large polar cap absorption events, in July 1959, the same behaviour was observed at Scott Base, Antarctica. These observations cover six polar cap absorption events, indicating that this behaviour is not unusual.

Comparison with all-sky camera films shows that most of this energy does not arise from visual auroral forms, since, during many of the exposures at the height of the storms, no auroral forms could be seen in or near the zenith.

The onset of the increased nitrogen emission is closely associated with the beginning of the polar cap absorption. Throughout this absorption the *D*-region ion density is well above its normal level, which implies that a large flux of ionizing and exciting particles is penetrating down to heights of 65 km. and lower[1].

At Thule the observations begin and end when the Sun is illuminating the atmosphere down to 100 km. in the zenith. During normal days the emission at 3914 Å. shows considerable twilight enhancement (shown in Fig. 1*b* by dotted lines which are exposures during which the solar depression is less than 18°). During the great storm enhancements no twilight enhancement is evident, suggesting the emitting region is below 100 km. The storm enhancement is so great that the normal twilight enhancement at these times would not be apparent. At Pole Station, in Fig. 1*a*, the Sun is at a constant solar depression of approximately 18°, so no twilight effects occur.

The forbidden O1 lines at 6300 and 5577 Å. do exhibit enhancements during the main phase of the magnetic storm, but they do not exhibit the steady changes over a period of days like the molecular nitrogen emissions. The Vegard–Kaplan bands of nitrogen are not observed in these spectra. These emissions are all from metastable states which would be collisionally deactivated below 100 km. The molecular oxygen bands are also present in the spectra. These factors suggest that the source of emission is near or below 100 km.

This work has been supported by a U.S. National Science Foundation grant through the Arctic Institute of North America. The co-operation of the staff of the Air Force Cambridge Research Laboratories is gratefully acknowledged.

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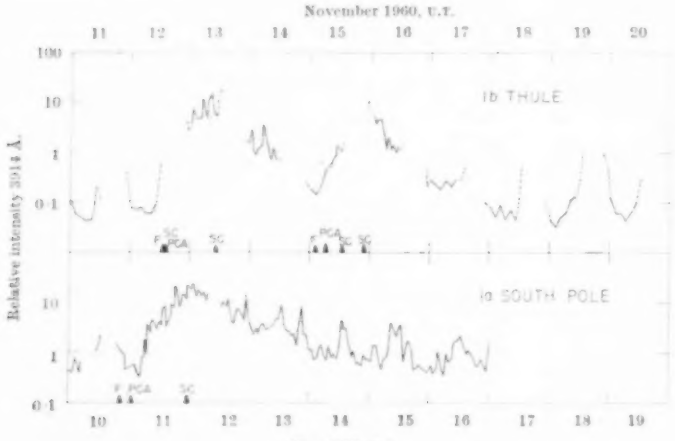

Fig. 1. The relative intensity in the zenith of 3914 Å. radiation at South Pole Station from May 10–16, 1959, in Fig. 1*a* and at Thule from November 11–20, 1960, in Fig. 1*b*. Times of major flares, polar cap absorption commencements and magnetic storm sudden commencements are indicated

ASTROPHYSICS

Origin of Cosmic Rays

Although cosmic rays have been known for more than forty years, their origin has not been satisfactorily elucidated. At present, it is believed that primary cosmic rays comprise nuclei of heavy elements ≈ 1 per cent apart from protons and α-particles. The presence of cosmically rare elements, for example, lithium, beryllium and boron in cosmic rays is of considerable importance for any theory of their origin. The other characteristic of cosmic rays is the energy spectrum which is of the form:

$$I(E) = KE^{\gamma} \qquad (1)$$

where I is the intensity of a given kind of particles and E is the total energy of a proton or nucleon. Here γ varies between 1·9 and 3·0, depending on the energy range. Their energy lies between 5×10^8 and 10^{18} eV. They also show in general the isotropy. The small anisotropy is, however, generated by the local sources and the local magnetic fields.

It is generally believed that the acceleration of ions in astronomical objects is caused by the interaction of the electric charge of ions with the local magnetic fields and not from nuclear or particle decay. Several acceleration mechanisms for the cosmic ray particle have been discussed in the literature, but none of them satisfactorily takes account of the whole range of the energy spectrum. I am of the opinion that not a single mechanism is involved, but a multiple process depending on the environment. Alfvén[1] has discussed the possibility of solar origin for the cosmic radiation. The theory is in good accord with most of the observed phenomenon, for example, the variations of cosmic rays in relation to various solar features, etc. However, it needs revision which has been deferred for future publication. On the other hand, Fermi[2] developed the theory of acceleration of cosmic dust through interstellar space. The cosmic particles are accelerated in interstellar space by moving magnetic fields. The longer the particle moves in interstellar magnetic fields, the greater will be its energy. From elementary considerations, he obtained the energy spectrum of the form of equation 1. However, this mechanism can accelerate only those particles the energy of which

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Appendix — Index

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8. **Difference between Averages**
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10. **Humidity and Moisture**
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12. **Cotton Fiber Length Analysis**
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15. **Non-Lint Content and Nep Potential**
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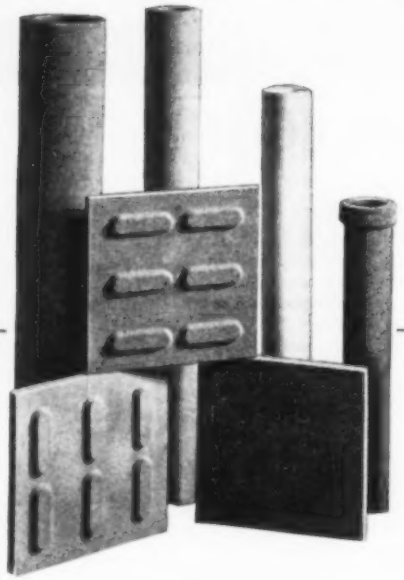

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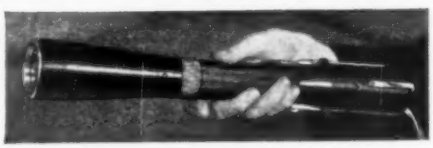

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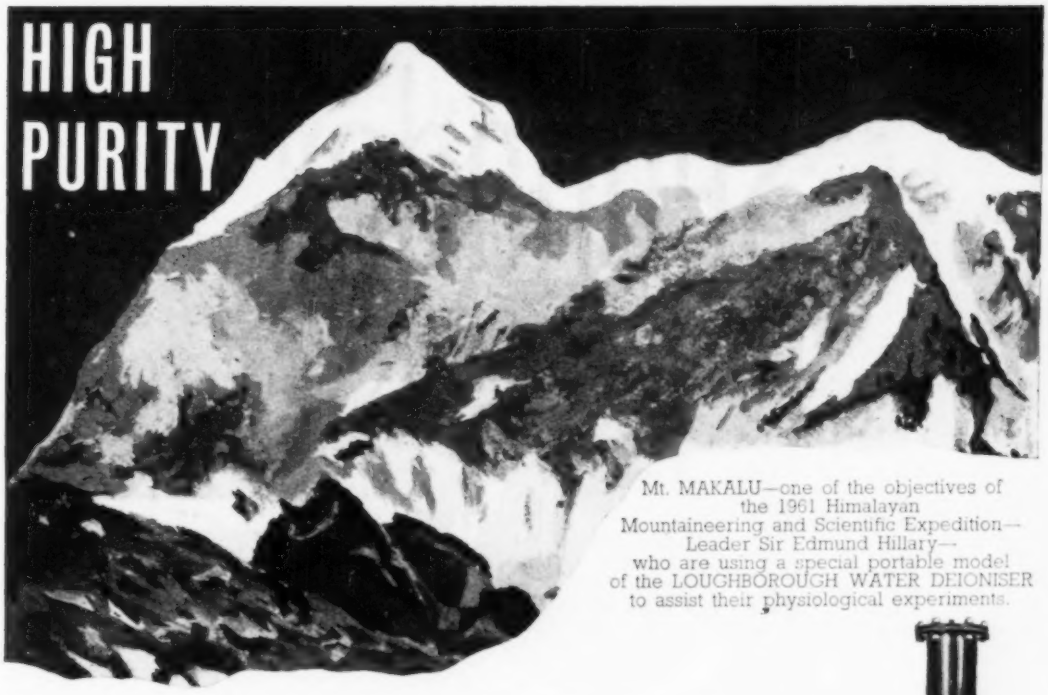

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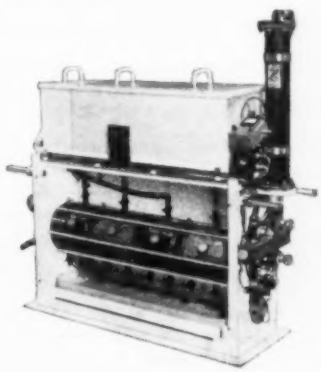

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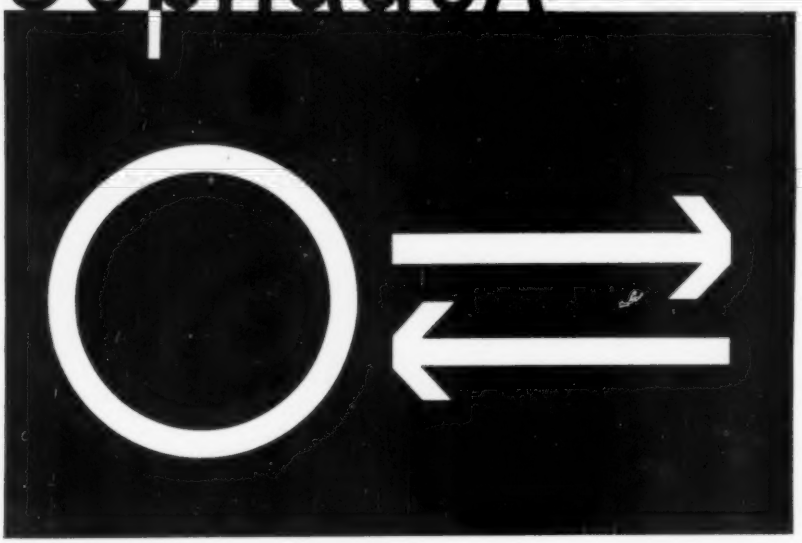

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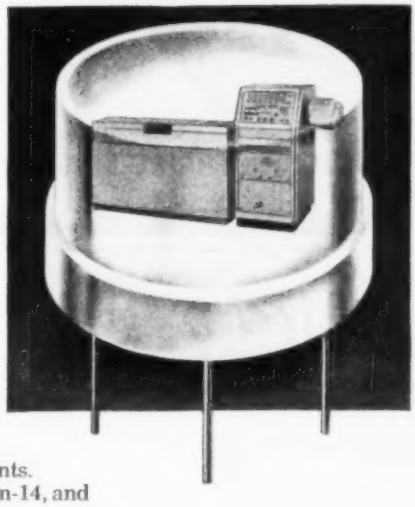

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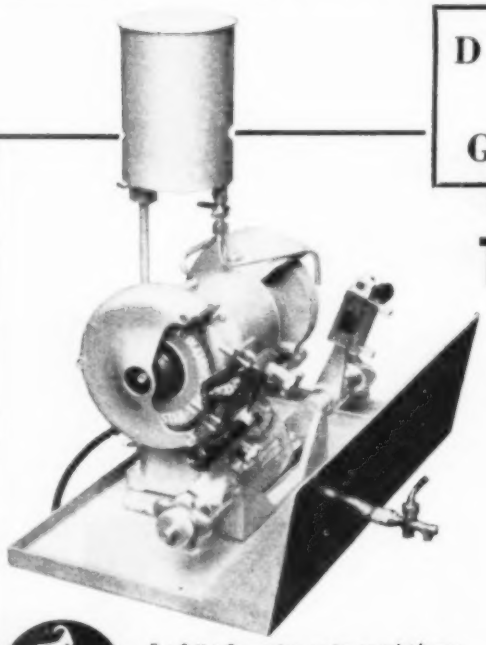

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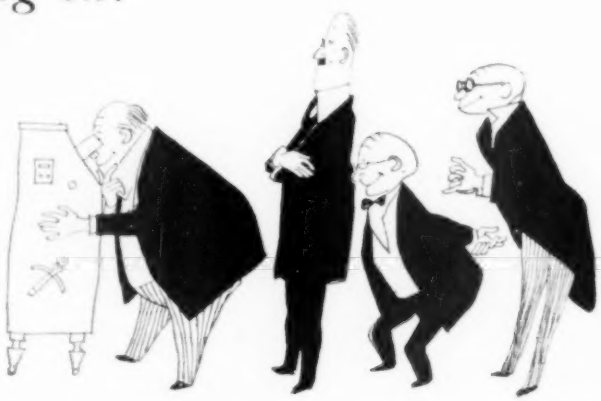

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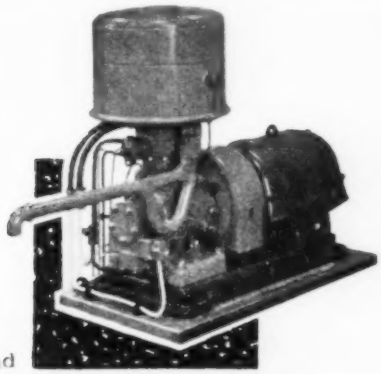

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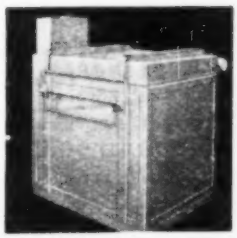

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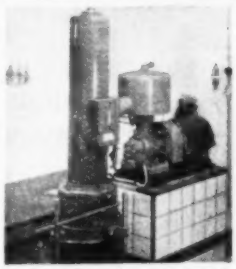

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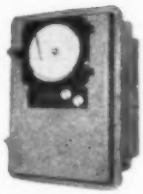

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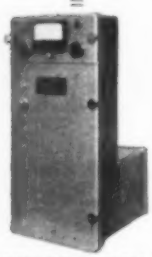

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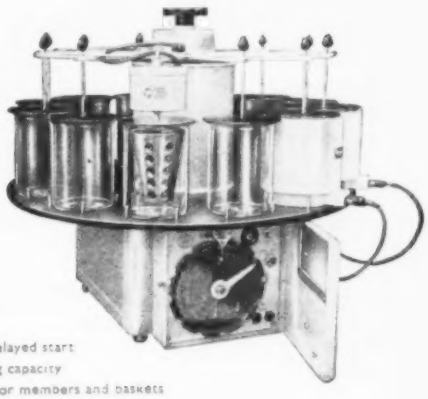

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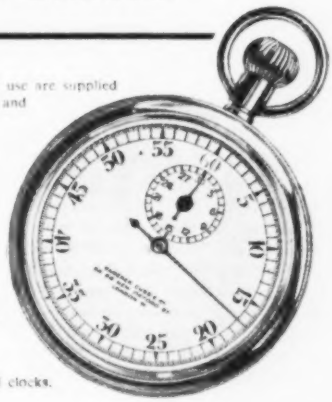

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The Effects of Ionizing Radiation in Liquid Systems - V

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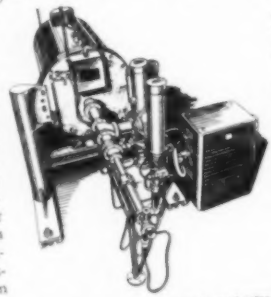

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Experimental Techniques

The experimental techniques usually adopted to study radiation effects are: measurement of the change of some solute in solution, or measurement of the yield of some product formed by the action of radiation. Analyses of radiation-formed products can be used to develop a mechanism for explaining the interaction of the incident radiation. Several Van de Graaff® accelerators, including those at the University of Notre Dame and the Brookhaven National Laboratory, are presently being used in studies of liquids under electron or x-ray bombardment.

Water Studies

One of the best-known liquids, which has received a great deal of attention from radiation chemists because of its importance in many radiobiological and radiochemical systems, is water. The generally accepted result of the interaction of a charged particle with a water molecule is dissociation, resulting in the production of free H and OH radicals. These may combine to re-form water or the molecular products H_2O_2 and H_2, or they may diffuse from the site of their formation to react with solute molecules in solution[2]. Studies of the kinetic behaviot of these radicals have been important in analyzing many radiation-induced reactions.

A typical experimental method of studying the effects of these radicals is to investigate the radiation yield in the wet and dry states. This will give the percentage of radiation-induced changes caused by the transfer of radiation energy from the solvent molecules to the solute. The addition of scavenger molecules which compete with the solute for radicals will give some indication of the relative reactivity of the radicals.[3]

Energy Levels

Since the energy of dissociation of typical liquid molecules is of the order of tens of electron volts, while the energy transferred from the incident radiation may be many hundreds of electron volts, it is difficult to measure the direct effect on the individual molecules. Although values of ionization and excitation energy have been extrapolated from gas-phase studies, it is not easy to relate the effect of the molecular binding energy in the solution to the dissociation energy. About the best that can be done is to obtain as uniform as possible a distribution of radiation energy throughout the system and to assume that all secondary electrons have the same probability of interaction as the primary beam. The yield is then calculated in terms of the number of molecules changed per unit-energy input. The unit is the so-called G value which measures the number of molecules changed or formed per 100 electron volts.

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exceeds a minimal 'injection' energy (E_{inj}), which for protons in interstellar space is $\approx 10^9$ eV, and for iron nuclei, 5×10^9 eV./nucleon. Further, Alfvén's theory cannot account for the particles of energy $> 10^{15}$ eV. Thus there must be some sources inside the galaxy which somehow generate particles of energy exceeding E_{inj}. The particles carrying great energies abandon their sources and are released into interstellar space, where they move in galactic magnetic fields for hundreds of millions of years and become accelerated by Fermi's mechanism.

The solar flare of February 23, 1956, is of considerable interest. During this flare, particles of the energy-range 10^9–$2{\cdot}4 \times 10^{10}$ eV. were observed. Simpson[3] found the total energy of the flare to be well in excess of 10^{32} ergs. These flares may be much more frequent in red dwarf stars as compared with the Sun and may in fact be the source of cosmic ray generation. In particular, the flare stars of spectral type *dM3e* (*UV* Ceti) and later, are very numerous. Perenago, as quoted by Shklovsky[4], believes that red emission dwarfs constitute a considerable fraction of the entire population of red dwarfs, the most abundant stars in the galaxy. It is possible that essentially all red emission dwarfs are flare stars to some extent. During the flare of *UV* Ceti stars, which lasts for several minutes, the luminosity rises by a factor of about ten. The flare occurs from once to several times a week. Thus the flare phenomenon on such stars is of the same general character as on the Sun, but will be much more energetic. Shklovsky[4] found that the power of optical radiation in a red-dwarf flare will be some 300 times as great as for such large solar flares as that of February 23, 1956. Thus the total energy of the red dwarf flare will be well in excess of 3×10^{33} ergs.

According to Kuiper[5], 81 per cent of the main sequence stars are *M*-dwarfs. The total number of stars of a galaxy are $\approx 2 \times 10^{11}$ and about 95 per cent of all the stars in our galaxy belong to the main sequence. Thus the total number of *M*-dwarfs in our galaxy will be $1{\cdot}6 \times 10^{11}$. Let us now assume that 10 per cent of the *M*-dwarfs are emission stars accompanied by a flare and that the flare event occurs on the average once in a year. The total release of energy by all the *M*-dwarf emission stars will be $\approx 1{\cdot}5 \times 10^{28}$ ergs/sec. This estimate may be an order of magnitude or two less because of the conservative approximation. Shklovsky[6] found that about 10^{29} ergs/sec. are lost in the galaxy as a result of nuclear collisions with interstellar gas. Thus I conclude that red dwarfs will supply sufficient energy to maintain dynamic equilibrium of cosmic rays in our galaxy. The hypothesis is further supported by the presence of heavy nuclei in cosmic rays since the synthesis of elements is advanced in the stellar system.

I am grateful to the University Grants Commission, India, for the award of a senior fellowship.

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METEOROLOGY

Numerical Retracing of Atmospheric Events

For obvious practical reasons, all numerical integrations of the equations of atmospheric motion published so far have been made forward in time. To be useful, such numerical forecasts must be started from a position of uncertainty and extend up to, or beyond, the most clear-cut stage of the development in question. But the numerical approach can also be regarded as a method of experimenting with the atmosphere, and in that context the above procedure seems far from ideal. It would then be more logical to start from some well-defined point separating the initial and mature stages and to integrate forward and backward in time, possibly using different models for the two stages. Since the origins of atmospheric disturbances are often inconspicuous on the synoptic scale or obscured by lack of observations, the processes during the developing stage, and hence the results of the backward integration, would in general have the principal interest in this type of experimental work.

At first sight, a backward projection of atmospheric events seems to require the reversal of the large-scale flow—a major dynamical problem. However, the structure of numerical integration procedures offers a very simple means of reversing the direction of the time co-ordinate itself. All the procedures suggested so far make use of rates of changes, or 'tendencies', which are assumed constant during each time-step and are added to the values of the corresponding variables at time t to obtain their values at time $t + \Delta t$.[2] A reversal of the time-direction therefore requires merely that the tendencies be subtracted instead of added.

Owing to the use of non-centred differences, the subtraction of tendencies will not ensure a complete reversal of events; but the discrepancies between the results of forward and backward integrations evidently arise from comparable errors in both computations. Other elements of irreversibility are introduced by finite difference approximations, smoothing operations and boundary processes.

The last of these require brief discussion. Charney, Fjortoft, and von Neumann have shown[1] that conditions must be prescribed in detail for boundary points with inflow. Mathematical arguments were presented recently[2] in favour of relaxing this condition, but it seems likely[3] that the prerequisites for this are not generally fulfilled. Backward integrations can be expected to illuminate this point further, since the reversal of flow implied in the reversal of time should make it necessary to reverse also the boundary condition.

We have tested the arguments presented here by means of the barotropic model applied to 500-mb. charts for the Australian region. The first calculation took an existing situation 24 hr. forward in time and then brought it back to the starting point. There was a loss of minor details, but all major features were fully restored. Computational instability developed during the retracing calculation at the outflow boundary, and vanished when the boundary condition was reversed. This supports the validity of the classical argument[1], and was further confirmed by the second calculation.

In this a marked upper depression which had developed unexpectedly over western Bass Strait was traced backward for 24 hr. to a region of the Great Australian Bight, where the available observations could not have shown its existence. The calculation also indicated the presence of a depression over the southern Tasman Sea, where the analysis previously had shown only an indefinite trough.

These results suggest that the retracing of large-scale flow developments may also have practical utility. Even with the best of present-day networks, forecasts remain affected by the uncertainties of regions lacking observations. The backward integration procedure can be used to make the analysis in such regions dynamically consistent with that for the network area. This approach will be explored in detail when we test the performance of the barotropic and other models in the Australian region.

We are indebted to the Bureau of Meteorology for the 500-mb. charts used in this work, and to Dr. F. Loewe and Dr. F. A. Berson for helpful comments.

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Small-Scale Turbulent Diffusion in the Atmosphere

Clarenburg and Tang[1] recently published a communication under this title in which they compared observations of smoke cloud spreading made by Frenkiel and Katz[2] with the relationships t, and $(t + 3)^{(2-n)/2}$, where t is time after generation of the burst, and n describes the shape of the one-point Lagrangian velocity autocorrelation; n was assigned the value 0·26, following Sutton[3]. Before the conclusion by these authors about the results of this comparison can be accepted, two points must be made:

(1) The authors base their computation of the spreading of smoke puffs on Sutton's well-known diffusion theory. It was pointed out in 1946, by M. I. Yudine[4], who referred to Richardson's[5] work and to the paper by Obukhov[6], that Sutton's treatment describes average dispersion, computed with reference to a fixed space-point or axis; but it does not describe relative diffusion of particles about a centre of gravity which is itself at liberty to move with the turbulence, as is the case with a smoke puff. The point has been emphasized and clarified in papers by Brier[7], and Batchelor[8–10], and many others. Relative diffusion depends on factors additional to the single-point, Lagrangian velocity correlation and hence cannot be described correctly by means of the parameter n. The additional factors governing relative diffusion are: (*a*) the initial size of the smoke puff; (b) multi-point Lagrangian correlations. Arguing from Obukhov's dimensional theory of turbulence, Batchelor deduced that the dispersion of a smoke puff should be proportional to a power of t less than unity at first, and afterwards to $t^{3/2}$.

(2) Clarenburg and Tang compared their diffusion theory with Frenkiel and Katz's excellent series of observations of the diameters of nineteen smoke puffs. The experiments were made on two successive days, and consisted of 7–20 photographic puff observations per experiment, made at one-second intervals. When a smoke puff spreads, at first its visible diameter increases; but later a maximum is reached, followed by a rapid decrease to zero. This maximum diameter seems actually to have been recorded[2] for at least eight of Frenkiel and Katz's smoke puff observations; runs number 6, 7, 13, 16, 18, 20, 9 and 11. The observed puff diameter is clearly not the same quantity as the (root mean square) dispersion of diffusion theory. The dispersion increases with time indefinitely. It is for this reason that other workers, starting with Roberts[11] (and including Frenkiel and Katz) have interpreted the visible smoke puff outline as a line-of-sight integrated smoke concentration value. According to this interpretation, it was shown by Gifford[12] that Frenkiel and Katz's smoke puff data (among others) support the predictions of the theory of relative diffusion. The observed puff dispersion proceeds at first according to a power of time less than unity, as long as the influence of the initial puff size is still dominant. But after about 10 sec. (for these puffs), the dispersion, but not the puff diameter, is found to obey a $t^{3/2}$ law for the remainder of the puff's visible lifetime.

The high correlations of smoke puff diameter observations with the assumed dispersion law $(t + 3)^{0.87}$, obtained by Clarenburg and Tang, stem from two separate, unrelated effects, neither of which has been considered by them: (*a*) At first, smoke puff diameters do increase in proportion to a power of time less than unity; this initially slow spreading does not, contrary to Clarenburg and Tang's assumption, reflect the degree of turbulence present, or the shape of the one-point Lagrangian autocorrelation function. Instead, it reflects primarily the influence of the initial puff size, according to the prediction of the theory of relative diffusion. (*b*) Later, when the influence of the initial puff size decreases to zero, relative diffusion proceeds at an accelerating rate, that is, according to a power of time greater than unity. The puff diameters, on the other hand, reach a maximum and then actually decrease with time. This is, of course, a purely optical effect, and does not reflect any corresponding decrease in the real turbulent diffusion-rate. In fact, the higher the real turbulent diffusion, the more marked this latter effect should be.

For the above reasons, it is difficult to agree with the conclusion by these authors that their theoretical results are in good agreement with these experimental data.

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PHYSICS

Velocity of Light emitted by a Moving Source

THE theory of special relativity is based on two main postulates, namely, the principle of relativity and the principle of the constancy of the velocity of light. If it is assumed that Maxwell's equations are correct and obey the principle of relativity, then the principle of the constancy of the velocity of light follows. The experimental evidence usually quoted in favour of the second principle is de Sitter's analysis of double stars. However, the principle has not been confirmed by experiments carried out in the laboratory using terrestrial sources. The need for such an experiment has been stressed recently by Dingle[1]. If the velocity of light is to have the same numerical value in all inertial frames then the velocity of light must be independent of the velocity of the source of light.

Generally, π^0-mesons decay into two γ-rays each having energy ~ 60 MeV. if the π^0-mesons decay when they are at rest relative to the laboratory. If the π^0-mesons are moving relative to the laboratory when they decay, then the source of the γ-rays is moving relative to the laboratory. It is known that this motion changes the energy and frequency of the γ-rays corresponding to the Doppler effect. If the principle of the constancy of the velocity of light were not correct then the velocity of the γ-rays from π^0-decay should vary depending on the velocity of the π^0-mesons relative to the laboratory when they decayed. Hence, if the velocity of the γ-rays arising from π^0-decay were measured, then it should afford a direct laboratory test of the principle of the constancy of the velocity of light. Let the π^0-mesons be produced in nuclear interactions inside the crystal of one scintillation counter by charged primaries (for example, protons $\sim 10^9$ eV. from an accelerator). The ionization produced in the crystal gives rise to fluorescence which is converted into an electrical signal by a photomultiplier. Any π^0-mesons produced will decay in a time $< 10^{-14}$ sec. so that the time of production of the γ-rays can be taken to be the time of entry of the primary particle. Let one of the γ-rays produce an electron pair in a second scintillation counter spatially separated from the first. The ionization produced by the electrons causes fluorescence in the crystal which is converted into an electrical impulse by the second photomultiplier. The time delay between the two electrical pulses can be measured electronically by several methods, for example, the first pulse could be used to trigger an oscilloscope and the position of the second pulse noted. With a separation of one metre the time delay would be $\sim 3{\cdot}3 \times 10^{-9}$ sec. if c were equal to 3×10^{10} cm./sec. If the velocity of the γ-rays depended on the velocity of the parent π^0-mesons then this time delay should vary depending on the velocities of the π^0-mesons. The main experimental difficulty would be to be sure that the coincidences observed would be due to the above events. As a check, the scintillation counters could be placed inside a large cloud chamber so that it could be checked that only one primary entered the first scintillation counter and that an electron pair was actually produced in the second counter. From the energy and direction of the electron pair, as observed in the cloud chamber, one could calculate an approximate value for the velocity of the parent π^0-meson.

It is probable that some other nuclear or meson process might prove more convenient to use in practice. A possibility might be to use a K-meson beam. Sometimes a K-meson emits π^0-mesons which afterwards decay into γ-rays. If the K-mesons were passed through a series of scintillation counters the positions and time of decay of the K-meson could be determined sufficiently accurately. The γ-ray detector could be placed off axis at a distance from the K-meson beam and the time delay measured.

The fact that in principle the experiment could be performed is of considerable interest even if it proved impossible to carry it out in practice. It has often been suggested that a direct experimental check of the principle of the constancy of the velocity of light is impossible since one would have to assume it to be true in order to synchronize the spatially separated clocks. In the above experiment one would not use two clocks but two crystals and photomultipliers, which would feed electrical signals into an apparatus which measures time intervals and which need not move before and during the experiment. When the events occurred, electrical signals would be sent along electrical cables to the timing machine and the delay in the transmission of the information could be allowed for once and for all by placing the two scintillation counters close together, and sending charged particles through both crystals and adjusting the lengths of the connecting cables until the pulses from both counters arrived simultaneously at the timer. The crystals and photomultipliers could then be moved apart without changing the length of any connecting leads. The delay in the receipt of information after the events would remain independent of the separation of the detectors if the velocity of electromagnetic disturbances in the connecting cables is independent of the directions and orientations of the connecting cables and is not changed when the cables are moved about. The usual method of synchronizing spatially separated clocks, as discussed in the text-books, is to use light signals which are assumed to travel in straight lines. In the present case the signals from the events can travel in curved paths such that the delay remains independent of the separation of the crystals and photomultipliers; the actual timing mechanism is not moved. In fact, in order to check the second principle one need not adjust the zero as described above, but one need only observe whether or not the time difference between the pulses from the two counters is the same whatever the velocity of the parent π^0-mesons relative to the laboratory when they decay.

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Absolute Measurement of Average Energy lost by Very Soft X-rays per Ion Pair in Air

FIG. 1 gives a survey of measurements made so far of W, the average energy lost by photons and particles per ion pair in air. At energies exceeding 10 keV. W is practically constant. At less than 10 keV. a tendency to higher values of W is indicated. The fairly large discrepancies between some of the results, especially at low energies, caused us to carry out an absolute measurement of W with very soft X-rays[1].

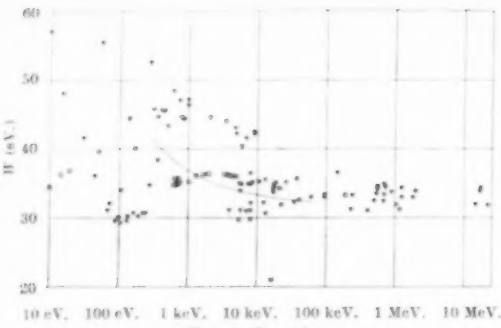

Fig. 1. W as a function of the energy. W for heavy particles is plotted in terms of the energy of electrons having the same velocity. ○, Photons; ▽, electrons; □, heavy particles

The measuring method is based on the equation, $W = nE_q/z$. The number n of monochromatic X-ray quanta of the energy E_q, produced by the filter difference method[2] has been measured by a total absorbing cæsium iodide scintillation counter. The crystal was enclosed in a container with a window of two aluminium foils, each 6·4μ thick, and mounted on the multiplier. The absolute counting was proved in preparatory experiments: the readings are independent (*a*) of the place of absorption in the crystal and (*b*) of the voltage across the electrodes of the photomultiplier in a certain range. The number z of ion pairs in air produced by the quantity of energy nE_q has been measured by a total absorbing standard ionization chamber[3]. The required corrections have been calculated and determined experimentally.

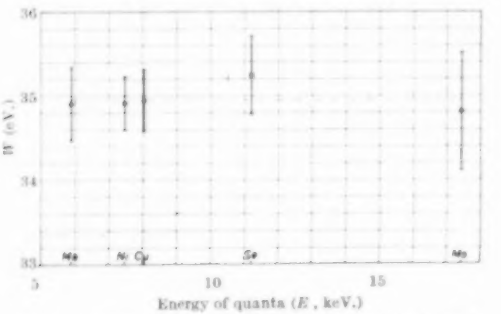

Fig. 2. Measured values of W with the standard deviation for each point. The mean value is also shown (broken line)

In a full analysis of the accuracy we found the following results (see Fig. 2 and also Fig. 1, marked ●): (1) there is no significant dependence of W on the quantum energy within the range, 5·89–17·44 keV.; (2) mean value of W is 35·0 eV.; (3) mean standard deviation is ± 0·5 eV.; (4) the method of measurement has maximum accuracy at energies about 7–8 keV.

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Similarity in Behaviour between Gas Bubbles in Liquid and Fluidized Solid Systems

Davidson *et al.*[1] have noted a marked similarity between the behaviour of gas bubbles injected into beds of solids which were gently fluidized and gas bubbles rising in a liquid. Within the narrow range of main fluidizing air velocity used for beds of glass beads, silver sand and swede seeds, the velocity of rise of bubbles, U, was found to depend only on the volume of the bubble, V, and agreed with the semi-empirical formula:

$$U = 0{\cdot}792\ V^{1/6}g^{1/2} \qquad (1)$$

derived by Davies and Taylor[2] for spherical capped gas bubbles in an inviscid liquid.

In this Department, using a γ-radiation absorption technique, the variation in voidage has been assessed when a measured stream of gas was injected into a similarly gently fluidized bed of 0·8 mm. diameter ballotini. The injection nozzle was clear of the base of the bed. It was found by calibration that change in observed count-rate was, to a first approximation, proportional to the change in voidage in the radiation beam over the voidage variation encountered. Thus it was possible to estimate an effective void residence time along the path of the radiation beam. By scanning the face of the column it was possible to measure an average projection of the voidage contours within the column and from this to measure directly the breadth of the injected disturbance—the bubble diameter. It was assumed that the bubbles were spherical on formation at the nozzle and then rose with the velocity given by equation 1; no allowance was made for interaction between bubbles in a chain. The bubble frequency to give the measured void residence time was calculated and Fig. 1 shows the relationship between this frequency and the rate of gas injection for two nozzle diameters (0·16 in. and 0·096 in.).

The general form of Fig. 1 shows that the bubble frequency, within the general scatter of results, is approximately constant at 22 per sec. for the higher injected gas-flow rates and that below injection-rates of 50 c.c./sec. there is a marked tendency for this frequency to rise. This is closely in accord with the results published by Calderbank[3] in a review of the behaviour of bubbles formed when air is injected into water through similar sized orifices. Thus these

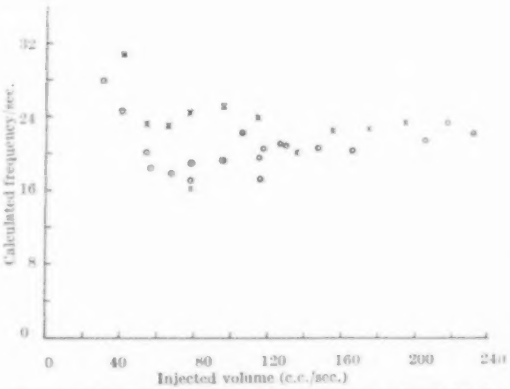

Fig. 1. Relationship between injected gas volume and calculated bubble frequency. ○, 0·16 in. diam. nozzle; ×, 0·096 in. diam. nozzle

observations also show a similarity in behaviour between gas bubbles in liquid and fluidized solids systems even though the actual mechanism of bubble formation in these two systems must obviously be quite different.

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Nucleation in Agitated Solutions

Mechanical disturbances are known to speed the onset of nucleation in supersaturated solutions. Early workers[1] demonstrated that severe mechanical shock could induce nucleation in metastable solutions at temperatures well above the so-called 'metastable limit', and more recent work[2] has shown that mechanical stirring can cause rapid nucleation in unseeded solutions which will not normally form nuclei under quiescent conditions. Published work to date has not given any indication of the effect of varying the intensity of agitation on the tendency of an unseeded solution to form nuclei under any given set of conditions, but it is generally assumed that more vigorous agitation increases this tendency.

Investigations carried out in these laboratories on nucleation and growth conditions in a pilot-scale Oslo crystallizer operating with unseeded solutions of ammonium dihydrogen phosphate have confirmed that the critical supersaturation, defined here as the degree of supersaturation at which nuclei are first observed in a solution being cooled at a constant rate, is dependent on the rate of circulation of the liquor, that is, on the degree of turbulence. Less supersaturation is required for nucleation to occur at the higher rates of flow.

It was observed, however, that at low rates of circulation, represented by Reynolds numbers of about 700–1,400 in a column of 3 in. diameter, the degree of supersaturation necessary for nucleation was not apparently reduced by increasing the turbulence. Unfortunately, variations in the value of the critical supersaturation were here of the same order as the experimental error. Accordingly, recourse was made to a smaller apparatus where conditions were more easily controlled. A glass *T*-stirrer was used in a small baffled beaker. The solutions of ammonium dihydrogen phosphate were covered with a thick layer of liquid paraffin and cured for about 30 min. at 10 deg. C. above their saturation temperatures before each run. Accidental inoculation by dust particles was thereby largely eliminated and reproducible results were obtained.

Whereas gentle stirring causes nucleation in solutions which are otherwise stable, and sufficiently vigorous stirring creates an even greater tendency to form nuclei, the transition may not be continuous; no simple relationship between the critical supersaturation and the intensity of agitation has been found. In general, a plot of critical supersaturation against rate of agitation is not a single smooth curve; in fact, a portion of the curve may have a reversed slope (see Fig. 1) indicating a region where an increase in the agitation reduces the tendency to nucleate. So

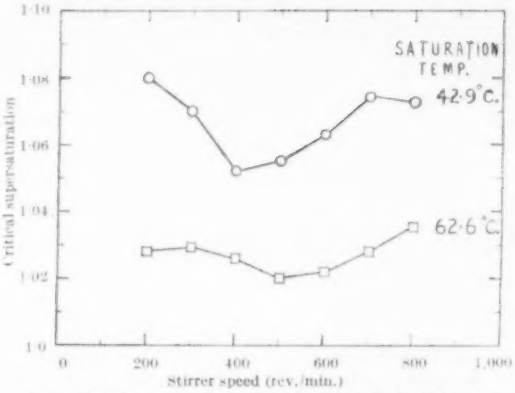

Fig. 1. Critical supersaturation (solution concentration/saturation concentration) versus stirrer speed for aqueous solutions of ammonium dihydrogen phosphate

far as is known, this is the first experimental evidence of such a phenomenon.

Nucleation in liquids has hitherto been considered as consisting of two stages: a diffusional transport step which is aided by agitation, and a surface reaction step when growth of the sub-nucleus occurs, the latter not being influenced by agitation. It would now appear that a third effect may also operate, which impedes the growth of, or disrupts, the sub-nuclei, and that this effect may predominate in certain circumstances.

The work, which so far has been confined to aqueous solutions of ammonium dihydrogen phosphate with saturation temperatures in the range 40–70° C., is being extended to cover a wider range of concentration and other solutes, to determine whether this effect is of general occurrence or specific to a limited range of conditions, and to attempt a theoretical explanation.

One of us (K. D. R.) is grateful to the Department of Scientific and Industrial Research for a studentship, during which this work is being carried out.

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Origin of the Word 'Neutron'

The word 'neutron' has been attributed to Rutherford by Glasson[1] and to W. D. Harkins[2] by Glasstone[3]. It appears likely that it was not used by either Rutherford or Hawkins before about 1920. In both cases, the neutron was a hypothetical combination of a hydrogen nucleus (also called a 'positive electron' or 'proton') and an ordinary negative electron.

I wish to point out that William Sutherland used the word in almost exactly the same sense in two papers published in 1902, in the first of which there is the passage[4]:

"As it would be convenient to have symbols different from the operational + and − to distinguish the two sorts of electrons, I propose to use the

musical types $\sharp$ for the + electron and $\flat$ for the − electron, and $\natural$ for the neutron, which consists of the $\sharp$ and $\flat$ united to form that electric doublet which gives to the æther its electric and magnetic properties."

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Phenomena occurring at Electrically Stressed Metallic Surfaces in Vacuum

CERTAIN hypotheses put forward to explain the mechanism of electrical breakdown of high vacuum, between metallic electrodes, rely on the removal from the electrode surfaces of aggregates of material[1,2]. Such aggregates have become known as 'clumps'. By means of radioactive layers on the electrodes or spectroscopic analysis, material transfer during the pre-breakdown phase has been shown to occur[3–5]. Breakdown has been initiated by the introduction of particles of electrode material in the gap[7]. The occurrence of points and pits on the electrodes has been confirmed by examining the electrodes microscopically before and after voltage stressing, while actual growth and tearing off of small points several μ in length has been photographed during an increase in voltage[8,9]. The latter observations showed that the points appeared to grow only on the anode, a fact supported by an observation that indicated the breakdown voltage was proportional to the tensile strength of the anode[10].

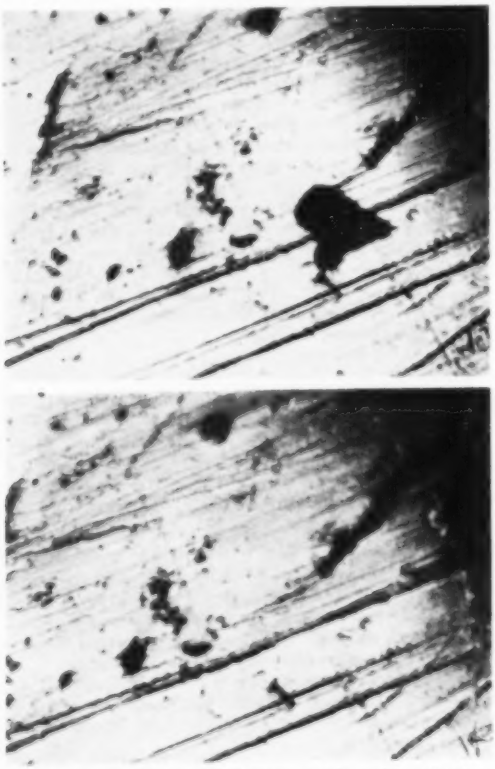

Fig. 1. Photomicrographs of copper anode surfaces showing the removal of an inclusion. Mechanically polished on 600 emery and then with metal polish. Gap 0·030 in. Pressure 8×10^{-5} torr. Top, zero volts; bottom, 10 kV. (× 550)

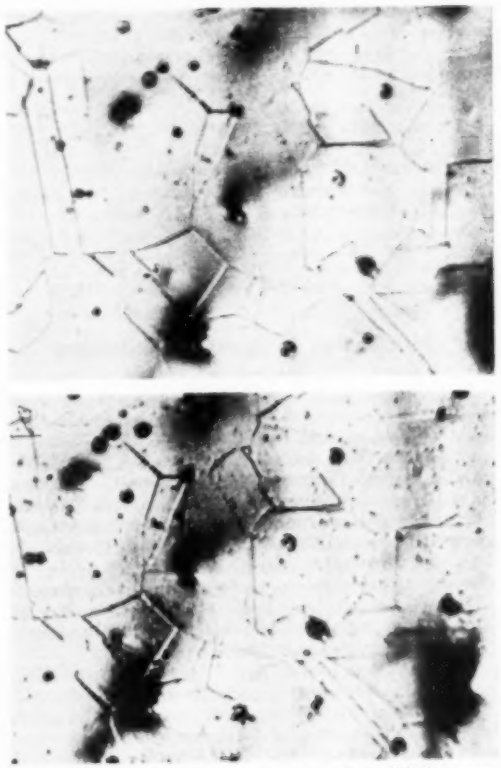

Fig. 2. Photomicrographs of electrolytically polished copper anode surfaces showing the appearance of 'spots'. Gap 0·015 in. Pressure, 8×10^{-5} torr. Top, zero volts; bottom, 24 kV. (× 550)

The actual observation of the growth of points was the first direct visual evidence that such multi-atom clumps were pulled out of the surface and transported across the gap. An apparatus was designed, before the foregoing results were known to us, in which the surface could be observed normally and with the voltage applied. It consisted essentially of an anode and cathode mounted in a continuously pumped vacuum cell. The cathode was in the form of a copper disk in the centre of which was a hole with bevelled sides, the diameter of the hole opposite the anode being 0·34 in. Located behind the cathode and in line with the hole was an 8-mm. objective lens, of 0·5 N.A., which fitted into a Vickers microscope. The anode was in the form of a 45° copper cone, the top of which was ground flat so that it just fitted the field of vision through the microscope. Analysis showed the copper to be about 99·5 per cent copper and 0·3 per cent oxygen with normal commercial impurities. Direct voltages were used and the breakdown current was limited by a 2-megohm series resistor. The pressure lay between 5×10^{-5} and 9×10^{-5} torr. Before some tests the anode was

polished with emery cloth down to 600 grade and then with 'Silvo' and finally washed in water, alcohol, and ether; in other cases it was electrolytically polished.

Some results of a preliminary series of tests are now reported as they confirm other investigators' results and give further information. With the gap set at 0·03 a large inclusion 2×10^{-3} cm. in diameter was seen to disappear from the anode at about 10 kV. or a 'stress' of $1·3 \times 10^{5}$ V./cm. Its removal did not cause breakdown. The effect is shown in Fig. 1, and although scratch marks can be seen from where the inclusion vanished they appear to be less intense than on either side of the inclusion. Thus it may well have been a piece of embedded cleaning material. Razin[9] also reports a clump tens of microns in size, being pulled off at a stress of 2×10^{5} V./cm.

In certain cases as the voltage was increased a different type of phenomenon took place in that 'spots' were seen to appear on the anode surface, as shown in Fig. 2. In the case shown the anode had been electrolytically polished, the gap was 0·015 in. and the spots arose at 24 kV. This corresponds to a stress of $6·3 \times 10^{5}$ V./cm. With the mechanically polished surfaces described earlier the spots arose at a stress of about 4×10^{5} V./cm. The size of the spots is about $1·5 \times 10^{-4}$ cm. diameter, which compares well with clump sizes estimated from the Slivkov hypothesis[2] of 5×10^{-5} cm. and with the smaller marks observed by Schwabe[8] of 2×10^{-4} to 5×10^{-4} cm. Cranberg[1] postulated the clump size to lie between 10^{-2} and 10^{-6} cm. The number of spots per square centimetre of electrode surface is of the order of 10^{6}. In several runs it took a further increase of voltage to cause breakdown but in others breakdown was immediate.

We wish to acknowledge the assistance of Dr. J. D. Meakin and Mr. R. A. Owen, Department of Metallurgy.

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GEOLOGY and MINERALOGY

Age of the Orogeny and Granites in South-West England

The Dartmoor and related granites form one of the key points in the revised geological time-scales of Profs. A. Holmes[1] and J. L. Kulp[2]. Therefore, their stratigraphic relationships need to be determined as precisely as the field evidence will allow. Kulp *et al.*[3] write that "while the Dartmoor granite is almost certainly post-Lower Westphalian, Lower Stephanian strata in Somerset are affected by the same fold system and it is therefore probable that the granites are of latest Stephanian or Permian age". It is by no means generally accepted, however, that the fold system in Devon and Cornwall is of the same age as that in the Somerset coalfield[4,5]. Indeed, Holmes[1] adopts a suggestion from Owen that the granites may have been emplaced in Upper Westphalian times and that the Pennant Sandstone of South Wales "may be the product of the rapid erosion of the rising Cornubian chains"[6]. A brief discussion of the available evidence therefore seems desirable.

The granites invade a folded and faulted stratigraphical succession in which, *at the present level of erosion*, the youngest sediments so far recognized by fossils are referable to the Upper Gastrioceras Zone of the Lower Westphalian[7–9]. It is likely, however, that a considerable tectonic thickness of deformed Palæozoic strata (perhaps many thousands of feet in the Dartmoor region) was originally present above the structures now seen[10] bordering the exposed granites. It therefore seems reasonable to suppose that even younger Westphalian, and perhaps even Stephanian sediments could well have been present in the deformed mass into which the granites were emplaced. Prentice's sedimentological conclusions from the Bideford area[11] support this view.

It appears that only unaltered Palæozoic rocks from the upper part of this deformed mass were being eroded in basal New Red Sandstone times[12]. Later New Red sediments contain contact-metamorphosed Palæozoic rocks, while the Lower Cretaceous Wealden sediments of southern England are thought to provide "the earliest evidence of the uncovering and denudation of the [Dartmoor] granite itself"[13].

It therefore seems preferable on the present evidence to regard the main orogenic movements in Devon and Cornwall as being of essentially the same age as those in the nearby Somerset coalfield, which are known to affect Lower Stephanian strata[14,15]. I support the assignment of the granites to the Permian[2] rather than to the latter part of the Carboniferous period[1]. The position of these granites in the geological time-scale will presumably affect the length of time to be allotted to the Carboniferous period, a matter of some importance in Carboniferous stratigraphy.

Thanks are due to Prof. A. Holmes for discussion in correspondence and to Prof. P. Allen, Prof. J. Sutton and Dr. R.St.J. Lambert for their comments.

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Attempted Low-Temperature Syntheses of Kaolin Minerals

Although kaolin minerals appear to be formed in Nature under acidic conditions at relatively low temperatures and low water-vapour pressures, their synthesis in the laboratory under similar conditions has been found exceptionally difficult. It appears that a proper choice of many variables is essential. In previous investigations[1,2], individual kaolinite crystals have been obtained by ageing mixed alumina and silica gels for 2 months at 100° C. and under *p*H conditions around 4·5, but the crystalline yield was extremely poor and the kaolinite could be proved only by single-crystal, electron diffraction methods; X-ray diffraction failed to detect the small yield. It seems that the ready polymerization of silica, with aluminium incorporated in the structure, inhibited the crystallization of a layer structure. Similar difficulties are not encountered in forming hydrous magnesian silicates.

Fig. 1. X-ray diffractometer patterns; copper *Kα* radiation. *A*, boehmite; *B*, boehmite obtained from gibbsite in sealed tube at 150° C.; *C*, gibbsite; *D* and *E*, gibbsite partially transformed to kaolin mineral; *F*, gibbsite wholly transformed to kaolin mineral

In the present experiments, gibbsite, $Al(OH)_3$, has been used as a source of alumina, together with silica either as a gel, 'Ludox', or in solution as ethyl silicate. The experiments have been conducted in sealed glass tubes at 150° C. and about 5 atm. water-vapour pressure, and with vigorous end-over-end agitation. The *p*H was controlled mainly by *N*/10 hydrochloric acid, but in experiments lasting 1–3 weeks the *p*H value often varied and a better control is desirable.

The results are illustrated in Fig. 1 by diffractometer diagrams. When the final *p*H exceeds 1·9, gibbsite is the only crystalline phase observed (cf. diagram *C*). When the *p*H remains below 1·5, a kaolin mineral replaces the gibbsite (cf. diagrams *D*, *E*, *F*). Electron micrographs show plate-like forms and also rod-like forms having some resemblance to halloysite. Reversible swelling and shrinkage behaviour is readily followed by X-ray diffraction, and each cycle of operations seems to improve the crystal structure. Whereas gibbsite in the absence of silica becomes transformed to boehmite at 150° C. under the conditions of the experiments (cf. diagrams *A* and *B*; also ref. 3), in the presence of silica the formation of boehmite is completely inhibited. Probably the instability of the gibbsite structure facilitates its reaction with silica to develop an alumino-silicate layer structure.

Further experiments are in progress in which temperature and *p*H will be controlled with more precision. This investigation forms part of Project 55, sponsored by the American Petroleum Institute.

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CRYSTALLOGRAPHY

Spiral Formation on Natural Crystalline Sulphur

Recently, observations of the growth spirals suggested by Frank's theory[1] have been reported on many different substances.

This communication records some interesting observations of growth spirals originating from screw dislocations on the (001) faces of natural sulphur crystals. The observations were made by means of an ordinary metallurgical microscope, using bright-field illumination. The heights of the steps were measured using interferometric techniques[2] and the values found range from 5000 Å. to 100 Å., showing that growth-promoting dislocations are of multiple strength.

Most of the faces investigated showed one spiral only, covering the whole area, which seems to prove that sulphur crystals must be extremely perfect.

Fig. 1 shows a spiral originating from a right-handed dislocation. Besides this elementary type of spiral, several other more complicated growth patterns, for

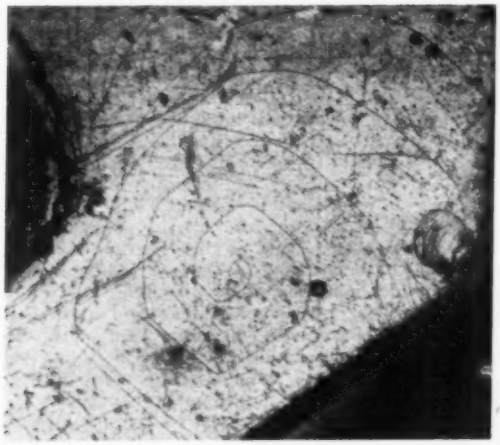

Fig. 1 (× 90)

two, three or larger numbers of dislocations ending on crystal faces, have been photographed.

The observed density of dislocations varies widely on different specimens, ranging from a few to a maximum of approximately 10^4 per sq. cm. On any one crystal they are predominantly of the same hand.

A more detailed account of these observations will be submitted elsewhere.

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Growth Spirals on Synthetic Magnetoplumbite Crystals

In connexion with a study of crystal growth from lead oxide and lead oxide–lead fluoride melts, we have recently observed growth spirals on (0001) faces of tabular magnetoplumbite ($PbFe_{12}O_{19}$) crystals. The spirals on crystals obtained from lead oxide–lead fluoride melts are polygonal, relatively open, and show concave growth fronts as well as reversed curvatures near the outer edges of the crystals. The step heights appear to be small multiples of the unit cell dimension in the c direction. The spirals on crystals grown from lead oxide melts are polygonized to various degrees, are more tightly wound, and exhibit greater step heights.

The magnetoplumbite crystals showing well-defined spirals were located on the top surfaces of melts from which yttrium–iron garnet crystals were grown by procedures approximating those suggested by Nielsen[1,2]. The spirals were observed with a petrographic microscope, using bright-field illumination. Fig. 1 shows a typical growth spiral on the surface of a crystal still attached to the top surface of a solidified lead oxide–lead fluoride melt. The small particles covering the crystal surface and decorating the step are believed to be flux components that solidified when the crucible was removed from the furnace (at about 1,000° C.). These particles were removed without otherwise altering the surface, by treating the surface with dilute nitric acid. Step heights were measured by a thin-film interferometric technique of the type described by Tolanski and Omar[3]. The value obtained for the height of the step near the origin of this spiral was 48 Å. The unit cell dimensions of a typical crystal (exhibiting a growth spiral) were determined to be $a = 5{\cdot}91$ Å., and $c = 23{\cdot}1$ Å., and the spiral was shown to be on the (0001) surface by X-ray methods. The step height (and Burgers vector of the screw dislocation(s) responsible for the spiral) on the surface of this crystal is approximately twice the unit cell dimension in the c direction. Dissociation of the spiral into two steps can be seen in the reversed curvature region (see below). The step height on a second spiral of similar appearance was determined to be about 68 Å., or approximately three times the unit cell dimension in the c direction. The displacement of interference fringes across the spiral step on many of the crystals was observable, but too small to measure. It is likely that these steps were a unit cell in height.

An interesting feature of the spiral shown in Fig. 1 is the partial reversal in curvature. A uniform supersaturation across the crystal face should lead to an equilibrium growth spiral that is approximately Archimedian in shape[4]. In the presence of concentration gradients, however, the shape of the spiral will be altered. An increase in supersaturation between the centre and the edge of a crystal face frequently occurs during crystal growth, and the suggestion has been made by Amelinckx[5] that a suitable gradient of this type may result in a complete reversal of spiral curvature. The spirals on magnetoplumbite crystals grown from lead oxide–lead fluoride melts have a shape that suggests a radial increase in supersaturation just sufficient to produce a reversal in curvature from about one-half of the radius to the edge of the face. The effect can be clearly seen in Fig. 2. Both right- and left-handed spirals are present on the surface of this crystal and both types show curvature reversals near the edge of the face. One can also see that the nearly straight segments of the spirals in Figs. 1 and 2 are slightly concave. The concave growth fronts may also be the result of an increase in growth-rate (supersaturation) with increasing distance from the centre of the crystal.

Numerous multiple-step spirals and complex systems of spirals were characteristic of the surface

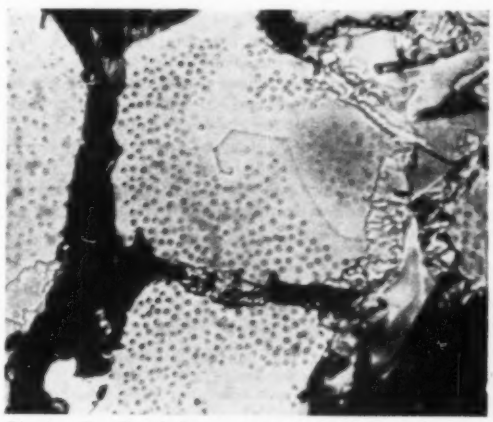

Fig. 1. Growth spiral on a magnetoplumbite crystal grown from a lead oxide-lead fluoride melt. (× c. 273)

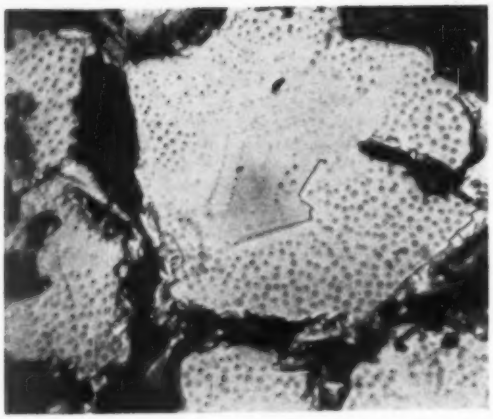

Fig. 2. Right- and left-handed growth spirals on a magnetoplumbite crystal. (× c. 273)

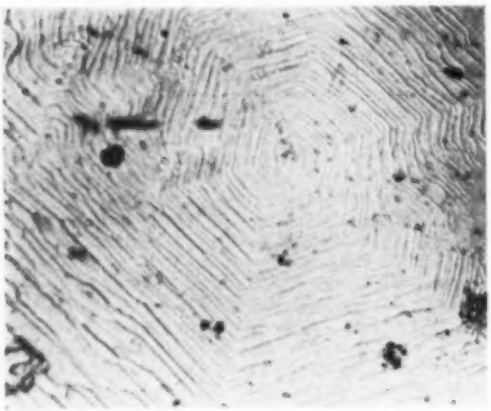

Fig. 3. Multiple-step growth spiral on a magnetoplumbite crystal grown from a lead oxide melt. (× c. 273)

features observed on magnetoplumbite crystals grown from lead oxide melts. Fig. 3 shows a tightly wound, multiple-step spiral on the surface of a crystal grown from a lead oxide melt. A value of 163 Å. (7 unit cells in the *c* direction) was obtained for the maximum height of a single step on this spiral. At higher magnifications, dissociation of the steps into smaller components was observed in several regions. The fact that these steps are more closely spaced than those observed on the faces of crystals grown from the lead oxide–lead fluoride melts is probably the result of higher supersaturations during growth. Such a result is consistent with the fact that magnetoplumbite is the major phase in the lead oxide system and a minor phase in the lead oxide–lead fluoride system.

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CHEMISTRY

Catalytic Activity of Coloured Alkali Halides

The properties of alkali halides containing colour centres are in some respects similar to those of semi-conductors: it was therefore thought to be worth while to determine whether such alkali halides have any of the catalytic properties of semi-conductors. The oxidation of carbon monoxide was chosen as a test reaction, as this reaction is readily catalysed by semi-conductors at low temperatures[1].

The halides investigated were sodium and potassium chlorides, potassium iodide and potassium bromide; all were of reagent grade purity and were used without further purification. The salts were thoroughly dried and ground, the portion between 150 and 300 mesh being used in the experiments.

Carbon monoxide was prepared by dehydrating formic acid with sulphuric acid, the gas being purified by passage through potassium hydroxide and magnesium perchlorate towers and finally through a liquid-air trap. Cylinder oxygen was passed through the same purification train, and probably contained traces of nitrogen and argon. A stoichiometric mixture of carbon monoxide and oxygen was used in all experiments.

The reaction vessel was a 'Pyrex' cylinder which could be fitted with a vapour-jacket for temperature control. The reactor, which had a volume of approximately 45 ml., was fitted with a thermocouple well, the end of which was always in the salt under investigation. Pressures were measured with both mercury and di-*n*-butyl phthalate manometers.

In a typical experiment, approximately 1 gm. of the ground salt was spread in an even layer over the bottom of the reactor. The reactor was then sealed into the vacuum system and heated to 250° C. for 10 min. at a pressure of less than 10^{-5} mm. mercury. The reactor was then brought to room temperature under vacuum, and dry air admitted to a pressure of 0·1 mm. mercury. The discharge from a Tesla coil was then played over the reactor for several minutes to produce colour centres in the salt. The reactor was then rapidly pumped out to a high vacuum ($<10^{-5}$), brought to the required temperature, and a sample of the carbon monoxide–oxygen mixture admitted. The manometer readings were followed as a function of time and, if the room temperature varied during the run, corrected for changes in the density of the manometric fluid. The manometer readings were also corrected for pressure changes in the non-thermostatted dead space of the reactor if there was any change in room temperature.

Experiments were carried out from 35° C. to 125° C. (above which temperature the colour centres bleached rapidly), with initial gas pressures of 10–250 mm. mercury. Runs were made both in the dark and in the presence of normal laboratory lighting. In no case was any evidence of catalytic activity obtained; although 0·2 per cent reaction in a 3-hr. period could have been detected. At the higher pressures a rapid, poorly reproducible decrease in pressure was observed immediately on admission of the gas. This decrease amounted to approximately 0·5 per cent of the initial pressure. This decrease could not be observed at the lower pressures, presumably because of drainage errors in the oil manometer.

Although the adsorptive properties of alkali halides have not been investigated in detail, it would seem from the work of Tompkins[2] that this pressure decrease might be due to a small adsorption of carbon monoxide. The work of Orr[3] suggests that oxygen adsorption would be negligible in the temperature-range of this work.

Experiments with the same gas mixture, in the same system, using nickel oxide as a catalyst, gave results comparable to those previously reported[1].

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Determination of Very Small Amounts of Hydrogen Peroxide

IT has been found that radiation doses of a magnitude as low as 10 r. damage cells in culture and interfere with their multiplication[1,2]. Although the damage is to be ascribed primarily to short-lived radicals produced by the rays rather than to the hydrogen peroxide also made, it is desirable to study the biological effects of small concentrations of this substance.

In this connexion, a very sensitive method for the determination of hydrogen peroxide is needed. The efficiency of ionizing rays in producing chemical species is measured by the G value, which is defined as the number of molecules formed per 100 eV. of energy absorbed. Using γ-rays (cobalt-60), G values for hydrogen peroxide production of 1·05–1·31 were found at dose-rates of about 3×10^3 r./min.[3–6]. Therefore, a dose of 10 r. will give in 1 ml. water hydrogen peroxide of about 10^{-11} mole ($\sim 3{\cdot}5 \times 10^{-10}$ gm.).

To develop a suitable method, we started from the report by Andreae[5] that scopoletin (6-methoxy-7-hydroxy-1,2-benzopyrone) is oxidized stoichiometrically (1 : 1) by hydrogen peroxide with loss of its fluorescence, provided horse radish peroxidase is present. The fluorescence before and after interaction with peroxide was measured with a Beckman spectrophotometer model *DU*, adjusted for fluorimetry. 10^{-10} mole of hydrogen peroxide could be measured. In the present work the determination was made with a Galvanek-Morrison fluorimeter, mark *V* (Jarrell Ash Co.), as usually employed for the determination of uranium in solid sodium fluoride pills. In this way, the sensitivity of the method has been improved by about one magnitude for the concentration, and by two magnitudes for the quantity of hydrogen peroxide.

The method was tested with hydrogen peroxide solutions. The solvent water had to be very pure to avoid spontaneous decomposition of the solute. Twice-distilled conductivity water was distilled three more times. First, with alkaline potassium permanganate; secondly, with silver nitrate; and finally, without any addition in a quartz apparatus. Hydrogen peroxide ('Perhydrol *p.A.*', Merck) was added to this water to give a solution about 0·2 per cent, and the exact concentration determined by iodometry. This stock solution was stable when stored in silica in darkness. For use it was diluted in steps, and the concentration measured by the scopoletin method after each step.

For the purpose, 0·1 ml. of scopoletin solution, 0·1 ml. of horse-radish peroxidase (C. F. Boehringer) solution (concentration not critical), and 0·1 ml. of hydrogen peroxide solution were mixed. The amounts of scopoletin were chosen so that at most three-quarters were used up by reaction with the hydrogen peroxide. 15 min. after mixing, 0·3 ml. of 0·15 *M* borate buffer (*p*H 10·0) was added, exactly one-half of the mixture transferred to a platinum dish, and the fluorescence measured. To obtain the fluorescence of the intact scopoletin, a blank mixture was made by including 0·1 ml. water instead of the same amount of hydrogen peroxide solution.

In Fig. 1, the logarithm of the number of moles of scopoletin oxidized (S_{ox}) is plotted against the logarithm of the number of moles of hydrogen peroxide as calculated on the basis of the iodometry with the stock solution. Clearly the method is applicable over a large range of concentrations. In Fig. 2, the destruction of the fluorescence in aliquots of one and the same scopoletin solution (containing initially $3{\cdot}12 \times 10^{-11}$ mole) by varying quantities of peroxide is shown, and Fig. 3 contains a similar plot for an initial concentration of $2{\cdot}5 \times 10^{-12}$ mole. It will be noted that the inclinations of the straight lines in the graphs are exactly 45°, as required by the stoichiometry 1 : 1.

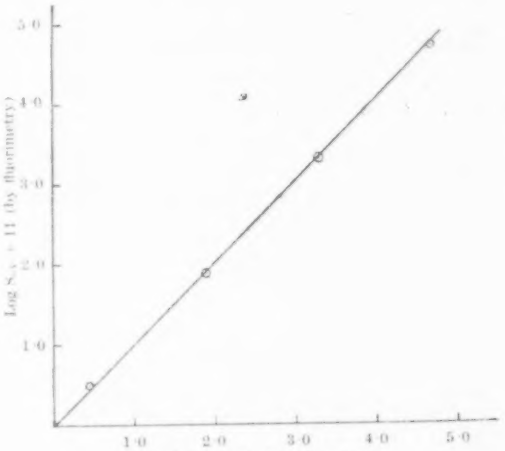

Fig. 1

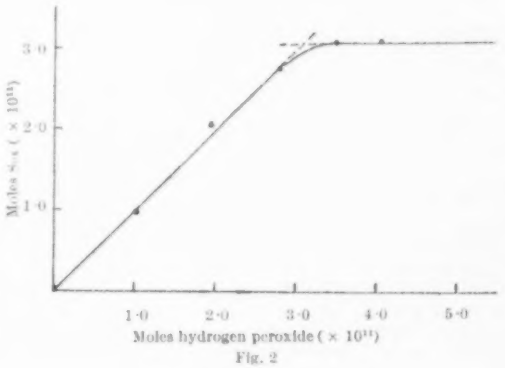

Fig. 2

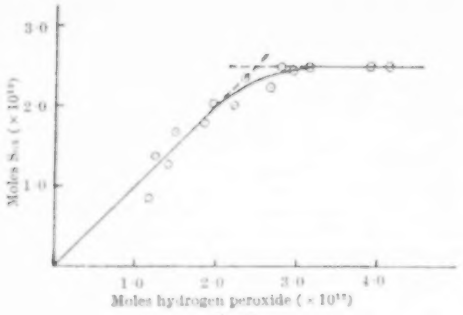

Fig. 3

It appears that in the range covered by Fig. 3 the limit of the method is reached. The scatter of the points in the lowest range is due to the fluctuations of the instrument when it works at its highest sensitivity. By proceeding statistically, that is, by measuring several identical samples in parallel and taking averages, the limit could be pushed down a little further.

In the method as used, the standard error is about 10 per cent in the measurement of $1{\cdot}5 \times 10^{-12}$ mole hydrogen peroxide, corresponding to a concentration of $1{\cdot}5 \times 10^{-11}$ mole/ml. in the initial solution, and to a radiation dose to this solution of about 15 r. Presumably even smaller concentrations and doses could be determined if the fluorimeter were adapted to take larger samples, or if the hydrogen peroxide could be diluted to a lesser extent by the reagents before measurement.

We thank the Jane Coffin Childs Memorial Fund for Medical Research for a grant and the Osterreichische Studiengesellschaft fur Atomenergie for the loan of the fluorimeter.

Note added in proof. By using more concentrated reagents, solutions of 5×10^{-12} mole/ml. have now been measured, corresponding to a dose of about 5 r.

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Electron Spin Resonance Line-Widths in Solutions of Copper and Silver Dithiocarbamates

In previous publications the electron spin resonance data of dithiocarbamates of the coinage metals ($[RR'NCS_2]_2Me$; Me = copper, silver or gold) have been used for a determination of valence states of the metals[1] and in a discussion of the bonding of the metal ions[2]. The copper and silver compounds exhibit very low effective spin-orbit coupling energy with small resonance anisotropy and unusually narrow lines. The small line-width makes it possible to analyse the influence on the width from a number of factors, and we shall briefly report on the effect of temperature, of dissolved oxygen and of different solvents.

In a liquid, where the paramagnetic molecules tumble at a sufficient rate, the position of the lines will mainly be determined by the isotropic parts of the spin Hamiltonian. However, in the cases where the hyperfine structure is anisotropic, the line-width will be dependent on the nuclear magnetic quantum number m_I. A theory for this effect was first given by McConnell[3], who used the results obtained by Bloembergen, Purcell and Pound for the nuclear relaxation. Recently, Kivelson[4] has re-examined the problem starting from the treatment given by Kubo and Tomita. The contributions to the longitudinal relaxation (characteristic time T'_1) and to the transverse relaxation (characteristic time T'_2) are given by Kivelson as:

$$\frac{1}{T'_1} = \frac{4\pi^2}{h^2}\left[\frac{1}{15}(\Delta g\beta B_0)^2 - \frac{1}{5}\Delta g\beta B_0 b m_I - \frac{1}{40}(b m_I)^2 + \frac{7}{40}b^2 I(I+1)\right]\frac{\tau_c}{1+4\pi^2\nu_0^2\tau_c^2}$$

$$\frac{1}{T'_2} = \frac{4\pi^2}{h^2}\left[\frac{4}{45}(\Delta g\beta B_0)^2 - \frac{4}{15}\Delta g\beta B_0 b m_I + \frac{1}{8}(b m_I)^2 + \frac{3}{40}b^2 I(I+1)\right]\tau_c$$

The paramagnetic molecules are assumed to have axial symmetry. $\Delta g = g_\parallel - g_\perp$ is the g-value anisotropy and $b = 2(A - B)/3$ is related to the hyperfine structure anisotropy. B_0 and ν_0 are the static magnetic field and the microwave frequency at resonance. Rogers and Pake[5] showed that these formulæ correctly describe the frequency and the m_I dependence of the line-widths of the VO^{++} ion.

We have studied the dependence on temperature of the line-widths of acetone solutions of copper diethyldithiocarbamates ($\Delta g = 0{\cdot}065$, $b = -0{\cdot}79 \times 10^{-4}$ cm.$^{-1}$)[2]. The conditions for validity of the formulæ are well fulfilled; for example, $\Delta g/g = 0{\cdot}03 \ll 1$. The correlation time was estimated using the relation $\tau_c = 4\pi\eta_i r^3/3kT$ with $r = 3{\cdot}5$ Å. and where η_i is the viscosity[6]. ν_0 is about 9,130 Mc./s. Fig. 1*a* shows the variation with temperature of the width (measured between the points of maximum and minimum slope) of the $m_I = +\frac{1}{2}$ line for carefully deoxygenated solutions. In the low-temperature region the agreement with the calculated width ($= (1/2T'_1 + 1/T'_2)/\pi\sqrt{3}$) is good, but the fact that there is a minimum in the line-width at a certain temperature cannot be explained on the basis of anisotropy mechanisms alone. The exchange mechanisms suggested by Pake and Tuttle[7] and further developed by Kivelson[4] might provide an explanation for the increase in line-width with increasing temperature; but as their contribution to the width should be proportional to the concentration they probably do not account for the whole difference between the experimental and calculated widths. Spin-orbit interaction or mechanisms such as discussed by Al'tshuler and Valiev[8] might be responsible for the main part of the high-temperature width. All such phenomena should, however, be independent of m_I and from Fig. 1*b* it is clear that Kivelson's formulæ well predict the difference between the widths of two hyperfine lines. The contributions to the line-width from the quadrupole interaction as calculated by

Kivelson are also in general dependent on m_I, but for only one nucleus with $I = 3/2$, these contributions accidentally are independent of m_I.

Dissolved oxygen has a marked influence on the line-widths of both copper and silver dithiocarbamates. The width increases linearly with increasing partial pressure of oxygen while preserving the area under the absorption curve. From the solubility of oxygen in benzene[9] and the formulæ given by Bloembergen, Purcell and Pound[10] for dipolar broadening, the contribution from oxygen with $p_{O_2} = 760$ mm. mercury is estimated to be of the order of 0·1 gauss. Experimentally the result is about 5 gauss (the resonance of diphenylpicrylhydrazyl in benzene is also broadened by dissolved oxygen to about the same extent). The discrepancy again could be due to exchange effects and measurements at different temperatures should be carried out. However, the variation with temperature of the solubility of oxygen makes such experiments difficult.

There is also a solvent effect in the electron spin resonance spectra both on the widths and on the resonance parameters. The most pronounced effect

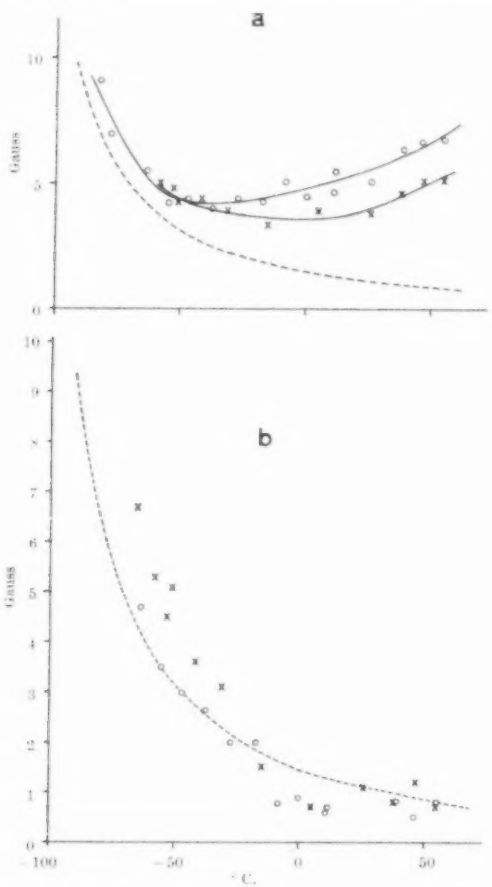

Fig. 1. Widths of hyperfine lines (measured between points of maximum and minimum slope) of 10^{-5} *M* and 10^{-4} *M* respectively acetone solutions of $[(C_2H_5)_2NCS_2]_2Cu$. Dashed curves are calculated from Kivelson's formulæ. *a*, Widths of $m_I = +\frac{1}{2}$ line; *b*, difference in widths between $m_I = -\frac{1}{2}$ and $m_I = +3/2$ lines. ×, 10^{-4} *M*; ○, 10^{-5} *M*

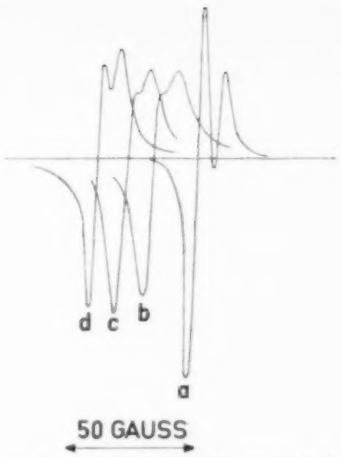

Fig. 2. $m_I = +3/2$ line of 10^{-4} *M* $[(C_2H_5)_2NCS_2]_2Cu$ in benzene–pyridine mixtures. The mole fraction of benzene is: *a*, 1·0; *b*, 0·9; *c*, 0·7; *d*, 0·0. Each line is an unresolved doublet due to the presence of two copper isotopes

we found in pyridine, where for $([C_2H_5)_2NCS_2]_2Cu$, the *g*-value is 2·0567 (in benzene 2·0453) and the hyperfine structure constant is $-0{\cdot}67 \times 10^{-2}$ cm.$^{-1}$ (in benzene $-0{\cdot}74 \times 10^{-2}$ cm.$^{-1}$). Similar solvent effects have been reported by Pake and Sands[11] and by McGarvey[12]. In mixtures of pyridine and benzene the lines have intermediate positions without appreciable broadening (Fig. 2), which shows that the exchange between solvent molecules close to the paramagnetic molecule must occur with a frequency higher than about $0{\cdot}5 \times 10^9$ c./s. This clearly demonstrates the inability of the dithiocarbamates to form complexes with pyridine as has also been demonstrated by chemical methods[13].

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Electron Spin Resonance Spectra of γ-Irradiated Carbohydrates and α-Hydroxy Acids

The production of polymers[1] from a wide range of carbohydrates and α-hydroxy acids induced by γ-irradiation of their de-aerated aqueous solutions posed the problem of identifying the monomer radicals responsible initially for such polymerizations. Measurement of the rates of dimerization of simple

hydropyranols[2] and the polymer yields from some twenty model carbohydrates[3] suggested that, with glucose, one of the primary reactions involved was a dimerization of the radical derived by abstraction of a hydrogen atom from the carbon of the hydroxymethyl group. The identification[4] of the radical obtained on γ-irradiation of polycrystalline glycollic acid, using electron spin resonance spectra, and the presence of the same radical in the liquid phase, inferred from the isolation of tartaric acid[5] from irradiated, de-aerated aqueous solutions of glycollic acid, suggested a close correlation between these systems. Moreover, recent work[6] on single crystals has enabled the proton coupling tensor elements for protons in certain environments to be determined accurately. With glycollic acid the peak separation (~61 Mc./sec.) of the polycrystalline sample corresponded closely with the average value (57 Mc./sec.) of the H(C) coupling which represents the isotropic part of interaction.

The polycrystalline carbohydrate and α-hydroxy acid samples were sealed off in evacuated glass phials (5 mm. × 20 cm.) and irradiated from a 180 c. cobalt-60 γ-radiation source for 15 hr. at room temperature. The samples could be kept at liquid-air temperature, until their spectra were recorded at ambient temperature on an X-band reflexion spectrometer[7] using small magnetic field modulation and phase-sensitive detection to present the first derivative of the absorption on a pen recorder. The magnetic field was swept comparatively slowly, taking up to 15 min. to record the spectra. The results shown in Table 1 were interpreted on the basis of the work of Whiffen *et al.*[8] and McConnell *et al.*[9] on irradiated single crystals. The spectra of 1-deoxy and 2-deoxy D-glucose could not be resolved.

Table 1

Compound	Type of spectrum and peak separation	Radical postulated
D-Glucose	doublet 42 Mc./sec.	—ĊHOH (carbon 6)
D-Mannose	doublet 35 Mc./sec.	—ĊHOH (carbon 6)
L-Rhamnose	doublet 14 Mc./sec.	>ĊOH (carbon 1, 2, 3 or 4)
D-Arabinose	doublet 8 Mc./sec.	>ĊOH (carbon 1, 2, 3 or 4)
D-Glucal	quadruplet 44 Mc./sec.	—ĊH—C< (carbon 1 or 2)
Mandelic acid	multiplet ~ 10 Mc./sec.	$C_6H_5\dot{C}(OH)COOH$
Hexahydromandelic acid	singlet 0	$C_6H_{11}\dot{C}(OH)COOH$

The spectrum obtained from D-arabinose is only consistent with hydrogen ejection from carbons 1–4 since ejection from C_5 would give a doublet with a peak separation of about 40–50 Mc./sec. L-Rhamnose appears to give a similar radical since a radical formed at C_6 of the type $>C—\dot{C}H_2$ would give a triplet (relative intensities 1 : 2 : 1) of total splitting 100 Mc./sec. while ejection of a hydrogen at C_5 would be expected to give rise to a quadruplet (1 : 3 : 3 : 1) of total splitting about 210 Mc./sec. (compare results frim 2-methyl malonic acid, Pooley, D., and Whiffen, D. H., unpublished results). The peak separation and anisotropic broadening observed with irradiated glucose and mannose are consistent with hydrogen ejection at C_6, resembling as they do the spectrum of polycrystalline glycollic acid. The quadruplet spectrum (relative intensities 1 : 3 : 3 : 1) of D-glucal can only arise because of hydrogen ejection at C_1 or C_2 with subsequent delocalization of free spin in the π-bond orbitals and interaction with the three protons—two on C_3 and one on C_1 or C_2. This result is consistent with the radical inferred from the identification of stable end-products from irradiated aqueous solutions in which hydroxylation and fission of the double bond were the predominant effects. The singlet spectrum of hexahydromandelic acid would be expected from a radical obtained by hydrogen ejection at the asymmetric carbon atom since any other radical would exhibit considerable α- or β-proton couplings. In the case of mandelic acid itself, the spectrum was also consistent with hydrogen ejection from the asymmetric carbon atom and subsequent delocalization of free spin and coupling to the aromatic protons, and here the total splitting of about 90 Mc./sec. was similar to that observed[9] in aromatic radical ions. Ejection of an aromatic proton was very unlikely.

Although the above results were obtained with polycrystalline solids and as such should be treated with reserve, in all cases they are in agreement with the radicals, which have been inferred from the isolation of stable end-products in irradiated, de-aerated aqueous solutions of these compounds.

We wish to thank the United Kingdom Atomic Energy Authority, Research Division, Harwell, for supporting these investigations and for a maintenance grant to one of us (H. D. S.), and Prof. M. Stacey, for his interest in this work.

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BIOPHYSICS

New Products from Wheat Starch, Flour and Gluten

Watson[1,2] has shown that graft polymers may be produced from certain substances of high molecular weight when they are masticated with monomers at ordinary temperatures in a machine in which high shearing forces are developed—the 'mechano-chemical reaction'. In the present work a laboratory machine of this type, invented by Watson[3], has been used to study the possibility of making, from different wheaten products, new substances of possible industrial importance.

In the first series of experiments, wheat starch or flour or gluten was masticated with a monomer,

for example, styrene, methyl methacrylate, acrylonitrile or methacrylic acid, in the presence of glycerol. In all cases a product of hard, rubbery to rock-like, consistency was obtained, the type depending on the duration of mastication. In a typical example a mixture of 71 per cent starch, 16·5 per cent styrene and 12·5 per cent glycerol was masticated for 30 min., and from this powder a hard, dense product was obtained.

There is evidence from the present work that glycerol does not merely give a suitable consistency to the initial mixture for shearing but also it participates in the reaction. Thus, new products have been obtained by simply masticating starch and glycerol without the presence of a monomer. For example, 85 parts of starch and 15 parts of glycerol in the masticator for 20 min. gave a tough, rubbery product, which became harder as the time of mixing was increased. In the reaction with starch, glycerol may be replaced by various glycols, for example, ethylene glycol, or by glyceryl monoacetate. It cannot be replaced by mono-functional alcohols or by glyceryl diacetate. Similarly, wheat starch triacetate will not react with glycerol.

Compared with wheat starch, the products have a low solubility and high paste viscosity. The evidence suggests, therefore, that an essential step in the formation of these products from starch is the cross-linking of the starch chains by a bifunctional reagent. Furthermore, products are obtained by masticating wheat starch with either diethanolamine or formamide. The nitrogen contents of the products indicate that, if cross-linking has occurred, there is about one cross-link per six anhydroglucose units when diethanolamine is used and about one in three with formamide. By contrast, cross-linked starches prepared by conventional methods[4] usually have one cross-link per 50 or more anhydroglucose units.

Gluten (washed out of flour and freeze-dried) behaves differently from starch or flour. Masticated alone, it shows no obvious change; but with glycerol or glycerol and styrene it yields a hard product. On the other hand, unlike starch, it yields a similar product with glyceryl diacetate. By contrast, casein gives a hard product with glycerol but does not react with glyceryl diacetate.

The products from mastication of starch and flour with glycerol and monomers are practically insoluble in aqueous solutions and in the common organic solvents over a wide range of temperature. They have approximately the same vapour-pressure isotherm as the parent starch or flour. They can be hot-extruded to give fibres of a brittle character, with a breaking strength of 400–1,100 lb. per sq. in.

Full details of this work will be published elsewhere, including an account of further experiments to decide if, in some cases, the mechano-chemical effect is not predominant but activates a thermal reaction. Watson[5] has evidence that in certain cases this can occur.

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BIOCHEMISTRY

Paper Chromatography of Hexosamines and N-Acetylhexosamines

An improved method of paper chromatography has been used to aid the separation of galactosamine hydrochloride from other hexosamine hydrochlorides in acid hydrolysates of chondroitin sulphate and to investigate the isomerization of N-acetylgalactosamine in alkaline conditions.

Barium chondroitin sulphate was prepared from dried bovine nasal cartilage by extraction with 1 *N* sodium hydroxide at 70° for 30 min. followed by neutralization and precipitation with 'Cetavlon'. Paper chromatography of fractions from 'Dowex-50' of hydrochloric acid hydrolysates showed the presence of glucosamine, galactosamine and an unknown amino-sugar. This amino-sugar was separated by re-elution from 'Dowex-50' with 0·3 *N* hydrochloric acid and identified as talosamine. Its hydrochloride was differentiated from galactosamine and mannosamine hydrochlorides and its N-acetyl derivative[1] from N-acetylglucosamine, N-acetylgalactosamine and N-acetylmannosamine by paper chromatography (Table 1) in butanol/pyridine/water (6 : 4 : 3). In the solvent of Fischer and Nebel[2] the mobility of the N-acetyl derivative relative to N-acetylglucosamine was 1·09, the same as that of synthetic N-acetyltalosamine[3].

Table 1. Paper Chromatography of Hexosamine Hydrochlorides and N-Acetylhexosamines

	Hydrochlorides		N-acetyl derivatives	
	A (cm.)	*B* (cm.)	*A* (cm.)	*B* (cm.)
Galactosamine	7·2	9·0	13·7	8·1
Glucosamine	8·1	10·9	14·9	10·4
Talosamine	7·9	11·5	16·1	13·3
Mannosamine	8·6	12·3	14·9	11·5
Solvent front	31·6	38·6	31·1	37·6

Solvent: Descending butan-1-ol/pyridine/water (6 : 4 : 3). Time, 16 hr.; temperature, 21°. Whatman No. 1 paper either (*A*) untreated or (*B*) with preliminary treatment in 0·1 *M* barium chloride. Sprayed for hexosamines and N-acetylhexosamines. Distances moved from origin (cm.).

Ninhydrin oxidation of the amino-sugar was carried out on the baso-line of paper chromatograms[4], which were then developed in butanol/ethanol/water (4 : 1 : 1) or in butanol/pyridine/water and sprayed with benzidine-trichloracetic acid reagent. The derived pentose was neither arabinose nor ribose, but coincided with the lyxose/xylose position. A similar chromatogram, after development in butanol/pyridine/water for 19 hr., was sprayed with 0·05 *M* borate buffer, pH 9·6, and subjected to ionophoresis at right angles, using a current of 0·4 m.amp./cm. width for 20 hr. Pentose markers had the following ionophoretic mobilities: xylose, + 13·3 cm.; arabinose, − 10·5 cm.; ribose, + 9·5 cm.; lyxose, + 7·5 cm. The derived pentose (+ 7·7 cm.) was clearly lyxose and the original unknown amino-sugar (not galactosamine) was talosamine.

The separation of the amino-sugars and of their N-acetyl derivatives was improved by preliminary treatment of the paper with 0·1 *M* barium chloride (Table 1), due partly to faster solvent movement and partly to variations in R_F. We find this procedure preferable to that of Fischer and Nebel[2] for investigation of mixtures of these compounds. Borate-

treated papers[1] give low R_F values for N-acetylhexosamines and N-acetylmannosamine coincides with N-acetylgalactosamine.

The isomerization of N-acetylglucosamine under alkaline conditions is known[5]. With 2 mgm. N-acetylgalactosamine and 0·125 ml. 1 per cent (w/v) potassium carbonate at room temperature for 2 days there was about 5 per cent conversion to a product corresponding to the previously identified N-acetyltalosamine. No further conversion was apparent after 4 days treatment.

N-acetyltalosamine was found to be present in a sample of N-acetylgalactosamine prepared by the acetylation of galactosamine hydrochloride derived from sheep tracheal cartilage[6].

These results do not necessarily mean that epimerization of N-acetylgalactosamine residues was responsible for the appearance of talosamine, because a high proportion of terminal residues would require to be epimerized during the alkaline extraction in order to give the talosamine (1 per cent of the total hexosamine) detected. If talosamine does occur naturally in cartilage, it may be associated with protein since purified chondroitin sulphate[7] contained no amino-sugar other than galactosamine and a neutral polysaccharide fraction[8] contained no amino-sugar other than glucosamine, but proof of its occurrence requires to be shown without use of alkali.

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Catalysis of Metalloporphyrin Formation: a Possible Enzyme Model for Hæm Iron Incorporation

Recent investigations on the incorporation of metal ions into porphyrins solubilized in aqueous detergent solutions have revealed two factors having a marked influence on the reaction-rate. The first is related to the charge on the detergent and has been termed the electrostatic effect; the second is concerned with the presence of certain chelating agents, and has been termed the co-ordination effect.

The electrostatic effect is such that the rate of incorporation of cupric ions (Cu^{++}) into dimethyl protoporphyrin ester is 20,000 times faster in 2·5 per cent sodium dodecyl sulphate than in 5 per cent cetyl trimethylammonium bromide under otherwise comparable conditions. This effect can be attributed to the electrostatic attraction of the cupric ions to the anionic micelle-water interface, where presumably they are able to interact with the nitrogen atoms in the tetrapyrrole nucleus. A possible structure for the solubilized porphyrin in which the pyrrole nitrogens are exposed to the aqueous phase is shown in Fig. 1.

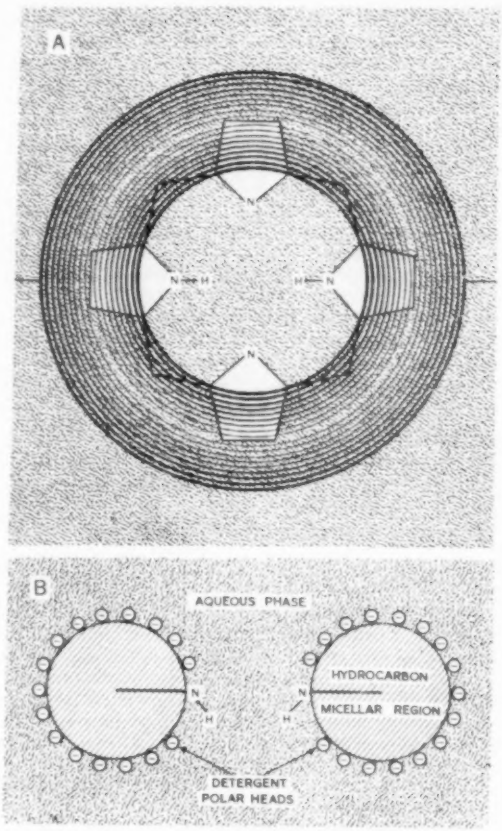

Fig. 1. A possible structure for the porphyrin – micelle complex with the porphyrin mainly immersed in the hydrocarbon region of the micelle and the nitrogen atoms in contact with the aqueous phase. *A*, plan; *B*, sectional view

The co-ordination factor is illustrated in Fig. 2, which shows the effect of increasing concentrations of 8-hydroxyquinoline (OX) on the initial rate of formation of copper protoporphyrin ester in a 2·5 per cent sodium dodecyl sulphate solution. It will be noted that the effect is maximal when the mole ratio of cupric ions to 8-hydroxyquinoline is 1 : 1, and that at higher concentrations of 8-hydroxyquinoline the rate is depressed. This suggests that the 1 : 1 $[Cu\ OX]^+$ complex is the active catalytic species. A similar effect has been observed in cationic and non-ionic detergent solutions. Because of the interplay of electrostatic and co-ordination factors in practice (one must, for example, compare the divalent cupric ion with the monovalent $[Cu\ OX]^+$ ion) it is difficult to assess the absolute catalytic effect of the co-ordination factor. However, it can be estimated to be 200–2,000-fold. The effect of other chelating and co-ordinating agents on the reaction-rate will be discussed in a further communication.

The temperature coefficient of the reaction (Q_{10}~2) is unaffected by the presence of catalytically

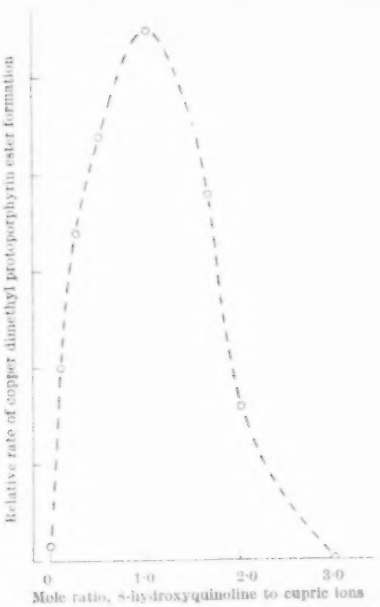

Fig. 2. Effect of varying the concentration of 8-hydroxyquinoline on the initial rate of formation of copper dimethyl protoporphyrin ester in 2·5 per cent sodium dodecyl sulphate at 40° C. The initial concentrations of cupric ions and dimethyl protoporphyrin ester were constant at 10^{-5} *M* and 10^{-6} *M* respectively. The *p*H was ~ 7·0

active [Cu OX]$^{+}$ species. This suggests that the co-ordination effect influences the probability of an effective collision (that is, the activation entropy) rather than the activation energy.

The maximum increase in rate yet observed from the combined influence of the electrostatic and co-ordination effects is 500,000-fold. This corresponds to the difference in initial reaction-rates between [Cu OX]$^{+}$ and dimethyl protoporphyrin ester in 2·5 per cent sodium dodecyl sulphate and cupric ions and dimethyl protoporphyrin ester in 5 per cent cetyl trimethylammonium bromide at comparable temperatures. Both effects have been observed to influence the rate of incorporation of ions other than cupric ions, for example, cobalt, nickel, ferrous iron and zinc.

The reaction studied in this system has features in common with an enzyme-catalysed reaction. Thus, the detergent solution, which consists of lipoidal micellar regions dispersed throughout an essentially aqueous phase, resembles the colloidal nature of the biological environment. The role of the detergent micelle in reacting with one of the substrates dimethyl protoporphyrin ester and simultaneously attracting the other substrate (cupric ions) to the same vicinity parallels the behaviour of an enzyme in bringing the reactants together—the porphyrin–micelle complex being analogous to an enzyme–substrate complex. The 8-hydroxyquinoline might be regarded as a co-factor which, by co-ordinating with one of the substrates (cupric ions) thereby facilitates the reaction. Both the electrostatic and co-ordination effects arise from changes in the entropy rather than the energy of activation, the electrostatic effect being associated with a concentration entropy term and the co-ordination effect with an orientation entropy term.

It is interesting to note that the large catalytic effect observed in this system has arisen solely from favourable changes in the entropy of activation. The importance of the entropy of activation in enzymic reactions has recently been pointed out[1] in connexion with the role of magnesium ions in enzyme syntheses involving adenosine triphosphate.

This hypothesis might have some relevance to the incorporation of iron in the biosynthetic formation of haem. Preliminary experiments have indicated that the rate of incorporation of ferrous ions into porphyrins in this system is several hundred-fold greater than that observed in other aqueous systems[2–4], although still considerably less than the known enzymic rate[5–7]. However, the relative magnitude of the effects discussed here is such that the enzymic rate of incorporation might yet be equalled by a further chemical modification of the system.

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Gastro-Intestinal Absorption of Heparin and Synthetic Heparinoids

Heparin and synthetic heparinoids have to be administered parenterally to assure clinical efficacy[1]. Since oral administration of these drugs would be highly desirable, numerous compounds were tested for their ability to effect absorption from the gastro-intestinal tract. The criterion of absorption was the appearance of plasma lipæmia-clearing activity, which was first described by Hahn[2].

Several compounds ('adjuvants') were discovered to have this property, the best of these being certain salts of ethylenediaminetetraacetic acid (EDTA). Other active compounds will be the subject of future communications. The present communication describes the use of salts of EDTA to obtain absorption of heparin and synthetic heparinoids.

Rats weighing about 200 gm. were placed in individual cages and fed for 72 hr. a liquid diet consisting of 30 ml. of a 33 per cent casein hydrolysate and water *ad lib.* The drug was given by intubation of an aqueous solution at a volume of 10 ml./kgm.

Table 1. Rat and Dog Lipæmia-Clearing Activity 4 hr. after Oral Sulphopolyglucin plus EDTA

Animal	No. of animals	SPG (mgm./kgm.)	Sodium salt of EDTA (mgm./kgm.)	Lipæmia-clearing activity (C.U.*)
Rats	5	500	—	0·04 ± 0·03
	5	500	500	2·41 ± 0·74
	4	—	500	0·01 ± 0·01
Dogs	5	100	—	0·59 ± 0·41
	6	100	50	5·73 ± 1·04

* Mean ± standard deviation

Table 2. Lipæmia-clearing Activity and Clotting Time after Oral Heparin plus EDTA in Rats and Dogs

Rats				Dogs		
Heparin Sodium salt of EDTA		50 mgm./kgm. 500 mgm./kgm.		Heparin Sodium salt of EDTA		100 mgm./kgm. 50 mgm./kgm.
Time (min.)	Clearing activity (C.U.*)	Clotting time (min.)		Time (hr.)	Clearing activity (C.U.*)	Clotting time (min.)
0	0·04 ± 0·03 (5)	7·0 ± 1·7 (16)		0	0·19 ± 0·18 (4)	11·3 ± 2·1 (8)
10	0·10 ± 0·09 (3)	11·0 ± 1·3 (3)		1	0·85 ± 0·70 (4)	>28 ± 21 (8)
30	1·46 ± 0·17 (3)	13·3 (2)		2	0·99 ± 0·66 (4)	>44 ± 22 (8)
60	0·31 ± 0·24 (3)	8·0 (1)		4	0·31 ± 0·45 (4)	18·1 ± 8·2 (8)

Figures in parentheses are number of animals. >, some animals had incoagulable blood (> 60 min.). *, Mean ± standard deviation.

At specified times, the rats were anæsthetized with pentobarbital sodium, and blood samples taken by cardiac puncture.

In dogs, after an overnight fast, the drugs were given orally in gelatin capsules. Blood samples were taken by venipuncture at specified intervals. Lipæmia-clearing activity of citrated plasma was determined[2] and expressed in clearing units (C.U.) calculated according to Grossman, except that incubation time was limited to 10 min., and the substrate was 'Ediol' (SchenLabs), diluted 1 to 50 with water. Whole-blood clotting time was determined by a three-tube Lee–White method[4] and indicated in minutes. When blood did not clot within 60 min., a value of 60 min. was used in calculating mean clotting time, but the '>' sign was added. All values for clearing activity and clotting time are given as mean ± standard deviation for groups of 5–10 animals or as specified.

The drugs used were heparin sodium U.S.P., potassium salt of sulphopolyglucin (SPG) and various salts of EDTA. SPG is a sulphated polysaccharide of 5 to 15 glucose units connected by α,1–4, and α,1–6 linkages, with 2–3 sulphate groups per glucose unit.

Typical experiments demonstrating the adjuvant property of sodium EDTA are presented in Table 1. Using lipæmia-clearing activity as an index of absorption, the results show, without question, the adjuvant properties of sodium EDTA. In dogs, where SPG alone produces measurable although somewhat erratic clearing activity, absorption of the heparinoid is increased about ten-fold by simultaneous administration of the sodium salt of EDTA. In rats, the effect of EDTA is even greater, since SPG alone is practically not absorbed.

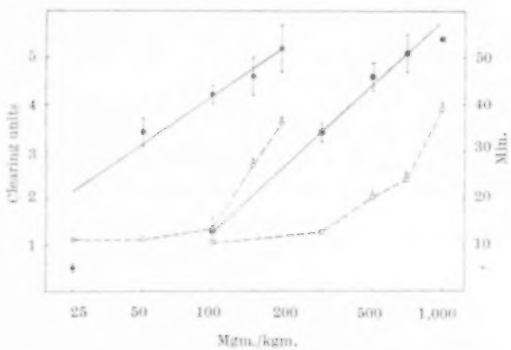

Fig. 1. Dose-response curves for lipæmia-clearing and anti-coagulant activities of SPG without and with EDTA in a ratio 4 : 1. Drugs given orally to groups of 5–10 dogs and blood taken 3 hr. later. Arrows indicate clotting times of more than 60 min. in some specimens. Limits in lipæmia-clearing curves are standard error. ●○, EDTA; ■□, no EDTA; ——, clearing; – – –, clotting

Similar results with SPG have been found in every animal species studied (monkey, dog, cat, rabbit and rat), as well as in man[5]. The adjuvant property of EDTA has also been demonstrated for other synthetic heparinoids (polyethylene sulphonate, dextran sulphate and others).

The adjuvant property of the sodium salt of EDTA can also be demonstrated for heparin, using both clotting time and clearing activity as criteria of absorption (Table 2).

The effects of EDTA are again unequivocal. In rats, clearing activity reached a peak about 30 min. after administration of the drug combination, and then declined slowly to control-levels. A similar time course was obtained for the anti-coagulant effect, with doubling of the clotting time at about 30 min. after the drug and subsequent return to control-levels. Since it is known that heparin is not absorbed from the gastro-intestinal tract, control experiments without EDTA were not made.

In dogs, the typical heparin effects appeared slower than in the rats. The peak of clearing activity and anti-coagulant effects were reached about 2 hr. after drug combination and returned to control-levels after more than 4 hr.

Further experiments were carried out in dogs to establish dose-response curves for SPG, both with and without EDTA. The results in Fig. 1 show good correlation between dose and clearing as well as anti-coagulant activity. Statistical evaluation indicated that the efficacy of SPG was increased approximately five-fold when EDTA, in the ratio 1 : 4, was used as adjuvant.

Significant amounts of heparin and synthetic heparinoids can be absorbed from the gastro-intestinal tract when these drugs are given orally together with an alkali salt of EDTA. The mechanism of this adjuvant effect is not clear. There is evidence that the chelation of calcium and/or magnesium ions by EDTA may be involved for the following reasons: (1) Sodium, potassium and ammonium salts of EDTA are effective as adjuvants; (2) calcium and magnesium EDTA are not effective; (3) adding a calcium salt blocks the adjuvant action of alkali EDTA; (4) phosphate buffers are not effective; (5) the adjuvant has to be given orally; intravenous injection of the adjuvant does not influence the absorption of SPG from the gastro-intestinal tract.

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Changes of Hexose/Hexosamine Ratio and Degree of Branching in Glycoprotein from Rat Urine during the Development of Cancer

We have isolated, from the urine of patients with cancer, an abnormal glycoprotein (III)[1] from fraction II (richest in carbohydrate, but low in sialic acid) of the Anderson–MacLagan glycoprotein (I)[2], which was characterized by a decreased hexose/hexosamine ratio, increased oligosaccharide-branching due to hexosamine and L-fucose residue and increased molecular weight, as compared with the exactly corresponding glycoprotein of urine of non-cancerous origin[1] (IV). These changes were observed, however, on fractions III and IV prepared from urine of patients with different stages of cancer, and also from normal and non-cancerous subjects[1]. We wished, therefore, to study those changes under comparable conditions, such as experimental cancer or inflammation, so as to follow up changes during pathological processes. But technical difficulties were great, since the yield of III is only 2–3 per cent by weight of I, and we were limited by the small quantity of animal urine available. It was observed, however, that the characteristic changes can be recognized even at the stage of purity of substance II.

Urine of four groups of ten rats (Wistar strain, female) were collected under toluene. The rats were inoculated intraperitoneally with ascites hepatoma 136 (Sasaki Institute, Tokyo), and afterwards pooled urine was separated every four days and substance II glycoprotein fractions were prepared; substance I from the pooled rat urine was solubilized with water at *p*H 8·4 (insoluble part rejected) and precipitated at *p*H 4·2, and centrifuged. The supernatant was electrodialysed for 3 days to effect complete precipitation, and the supernatant was lyophilized and analysed without further purification. In two groups of ten rats, inflammation was set up by intraperitoneal injection of turpentine oil, and the urine of days 2–7 after injection were taken, similarly treated and analysed.

Table 1. Changes of Glycoprotein Fraction II in Inflammation and during Development of Cancer

	Normal rats (before inoculation)	Inflammatory rats † (turpentine peritonitis)	Cancer-bearing rats * (ascites hepatoma 136, Sasaki)			
			Days after inoculation			
			1–4	5–8	9–12	13–death
Hexoses (ref. 3)	14·8	13·2	10·7	13·6	9·7	8·1
Pentoses (ref. 3)	5·3	3·1	3·0	4·0	3·5	3·2
Methyl pentoses (ref. 4)	3·4	3·2	3·0	3·2	3·2	3·4
Hexosamines (ref. 5)	8·1	8·1	8·4	10·9	8·5	9·1
Carbohydrate terminals (ref. 6)‡	5·6	5·5	4·6	6·5	8·1	8·1
Ratio of hexose to hexosamine	1·8	1·6	1·3	1·2	1·1	0·9
Ratio of total carbohydrate § to terminal carbohydrate	17·7	19·9	18·1	20·6	32·6	38·4

For methods of determination, see the corresponding references.
* Mean values of four groups of ten rats.
† Mean values of two groups of ten rats.
‡ Expressed as percentage of the amount of formic acid evolved on periodate oxidation for 12 hr. at 5° C.
§ Excluding sialic acid.

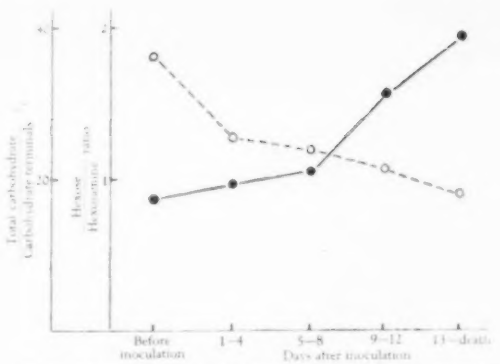

Fig. 1. Changes of degree of branching (full line) and ratio of hexose to hexosamine (dotted line) of the glycoprotein II from rats during development of cancer

As is shown in Table 1 and Fig. 1, the non-amino-to amino-sugar ratio decreased, and the ratio of the total carbohydrate to end-group carbohydrate increased with the development of cancer, but these ratios remained unchanged in the case of inflammation.

In view of the significant role of oligosaccharide branching and the hexose/hexosamine ratio in the determination of the biological specificity of muco-substances[7], it is considered that the lost hexoses and increased branching observed in the abnormal glycoprotein must reflect lost specificity of the normal molecule, and leads to the appearance of the structure responsible for pathological specificity.

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Fractionation of Compound Lipids by Dialysation in an Organic Solvent against an Organic Solvent

Compound lipids in general are not dialysable in aqueous solution or emulsion because they form micelles. Their dialysability in organic solvents, however, has not been examined in detail; but it seems to be largely dependent on the state of the organo-micelle[1]. It was therefore thought that by dialysation of individual compound lipids in organic solvents against successive changes of solvents of different polarity, the so-called 'high-molecular lipids'[2] or 'mucolipids'[2,3] would remain undialysable if they are really of high molecular weight.

We have examined the dialysability of various compound lipids in a number of organic solvents, and the following findings are of special interest: (1) Chol-

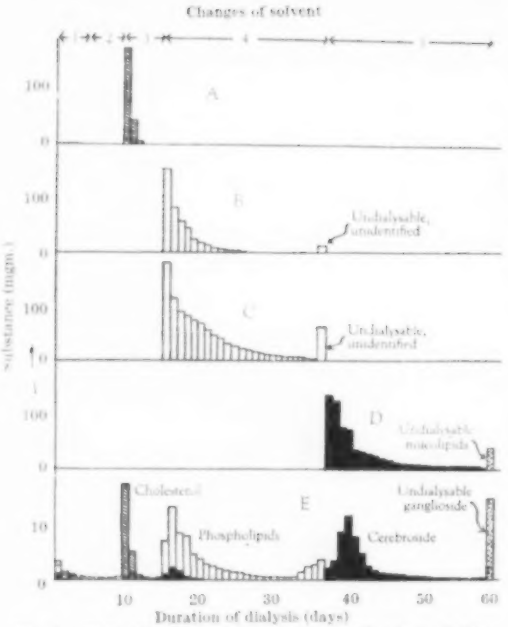

Fig. 1. Dialysability of cholesterol (*A*) in chloroform; I (*B*); mixture of II and III (*C*) in chloroform–methanol (2 : 1, v/v); IV (*D*) in pyridine and of a mixture of these with V (*E*). Dialysis was carried out by using a Visking tube, 1 cm. × 20 cm. against a 100-ml. aliquot of various solvents. Solvent 1 : benzene/petroleum ether (1 : 1, v/v). Solvent 2 : benzene/chloroform (1 : 1, v/v). Solvent 3 : chloroform. Solvent 4 : chloroform/methanol (2 : 1, v/v). Solvent 5 : pyridine. Temperature, 5 ± 1. The abscissa represents the duration of dialysis in days and the ordinate is the amount of substance dialysed in mgm. In experiment (*E*), 20–50 mgm. each of the mixed material dissolved in 30 ml. of benzene petroleum ether (1 : 1) placed in a 1 cm. × 40 cm. Visking tube were dialysed in 100 ml. of solvent

esterol, phosphatidyl-cholin (I), -ethanol amine (II) and -serine (III), and cerebroside (IV) can be dialysed in different polarity of the media used through Visking 24 A. membrane (see Fig. 1). A trace of undialysable portion was recognized in substances I–IV, even in chromatographically pure substances I–III (ref. 4), but the undialysable remainders of I–III have not been identified as yet. Ganglioside (V) prepared from strandin[5] fraction cannot be dialysed in any of the media.

(2) Substance IV, prepared from protagon[6], crystallized thrice from ethanol, twice from glacial acetic acid, can be separated into a dialysable fraction (VI) and an undialysable fraction (VII) by dialysation for two weeks in pyridine (outside liquid changed every day). Substance VII was separated into water-soluble supernatant (VIII) and gelatinous precipitate (IX) when dialysed against water (150 mgm. of VIII and 230 mgm. of IX from 6·5 gm. of IV).

The fast dialysable (within 2–3 days) fraction of (V) was identified as almost pure cerebroside by analysis ; N, 1·70; hexose, 18; P, 0·01; SO_4, 0·2 per cent; $[\alpha]_D^{25}$ in pyridine, 4·5°. The hydrolysate gave only galactose (a typical infra-red spectrum). The slowly dialysable (7–14 days) fraction of (V) contains mainly galactose and also a small amount of galactosamine, but no glucose.

From substance VIII was isolated by chromatography on cellulose[7], two main peaks eluated with methanol/chloroform/water (7 : 3 : 0·5 by vol.). They were typical of mucolipids but different from ganglioside[8] or 'brain mucolipid'[9]; they were characterized by strong dextro-rotation, ($[\alpha]_D^{25}$ in pyridine = +68° and +84° respectively), but both contain glucose, galactose, galactosamine and a trace of sialic acid. Substance IX has not yet been purified, but is believed to be a glycolipid linked with polypeptide (the hydrolysate gave such amino-acids as glutamic acid, aspartic acid, serine, glycine, leucine and valine); N, 3·5 per cent; hexose, 25; P, 0·8; sialic acid, 5·5 per cent. It is noticeable that only the undialysable fractions (VII and VIII) contain a considerable amount of glucose.

(3) Fractional dialysation of artificial mixtures of cholesterol, I, II, III, IV and V has been tried. Although up to the present simultaneous dialysation (co-diffusion) of a small amount of IV with the majority of II and III has been observed, almost successful separation of individual compound lipids has been accomplished, as is shown in Fig. 1*E*. Substance V, which is thought to be the only high-molecular lipid among these mixtures, has been recovered as the undialysable remainder.

This type of fractionation may be of considerable importance, since it does not include any drastic treatment and can resolve the individual lipids in their native state.

Full characterization of the individual fractions will appear in detail elsewhere.

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Fractions of Trypsinized Casein giving Different Patterns of Bacterial Growth

The rate of growth of a strain of *Streptococcus equisimilis* in a medium comprising acid-hydrolysed casein, glucose and yeast extract has been shown in these Laboratories to be markedly increased by the addition of a small amount of a tryptic digest of casein. While investigating this effect, which had been shown not to be due to the ability of the enzymic digest to supply free amino-acids, it was found to be possible by chromatography on paper in *n*-butanol/acetic acid/water (25 : 6 : 25 by vol.) to fractionate the digest in such a way as to separate compounds possessing growth-stimulating activity of two distinct types. Thus constituents of the digest possessing approximately the same R_F as that of glycine resulted, after a very short lag, in a sudden increase in the rate of growth of the organisms which, however, was of short duration (Fig. 1*a*). On the other hand, the effect of constituents of the digest with R_F values similar to that of valine reached a maximum only after a prolonged lag and differed again from the previous effect in that the high rate of growth was sustained (Fig. 1*b*).

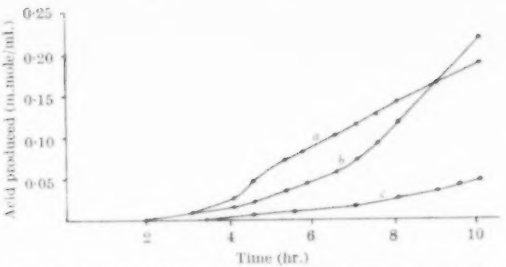

Fig. 1. Growth patterns of a strain of *Streptococcus equisimilis* showing effect of fractions of trypsinized casein separated chromatographically. For convenience, growth is expressed as m.mole/ml. of lactic acid produced. *a*, Basal medium + glycine fraction ; *b*, basal medium + valine fraction ; *c*, basal medium

It seemed almost certain from the protein nature of the starting material that the active substances in the casein digest were peptides, and indeed, an active peptide with the same R_F value as that of valine has now been isolated chromatographically from a tryptic digest of casein. The effect of this peptide was of the predicted type, as rapid growth-stimulation occurred only after a long lag period. Fractions obtained by filtration of casein digests through 'Sephadex *G*-25' (ref. 1) were further resolved by a two-dimensional technique involving the successive use of paper chromatography and high-voltage electrophoresis[2]. By these means, the presence has been confirmed of a great multiplicity of peptides in both the glycine and valine regions of chromatograms (Fig. 2).

It has been known for some time that certain natural or synthetic peptides exert a stimulatory effect on micro-organisms, particularly the *Lactobacilli*[3], while more recently, Kihara and Snell[4] have advanced the attractive theory that this stimulatory effect resides in the ability of peptides in some instances to overcome blocks in the metabolism of individual amino-acids.

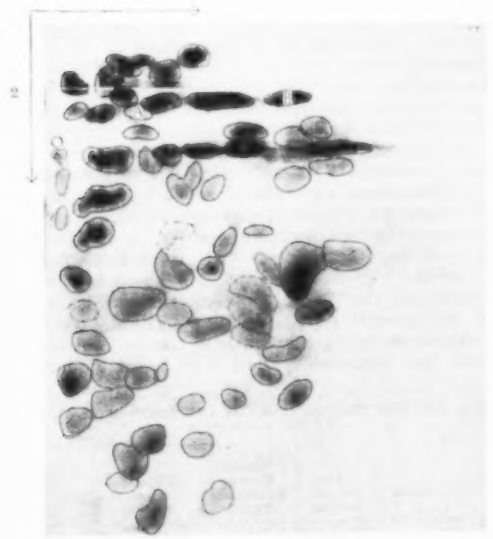

Fig. 2. Two-dimensional separation of peptides of trypsinized casein. 1, Chromatography in *n*-butanol/acetic acid/water ; 2, electrophoresis at 2,500 V. for 1 hr.. Phosphate buffer at *p*H 7·7, μ = 0·05. *A*, glycine ; *B*, valine ; *O*, origin

In the present work the diverse effects shown by the two peptide fractions might be interpreted as indicating the changing requirements of the bacterium for specific peptides at different stages of growth. On the other hand, it is possible that the present results relate to current theory as follows : Pattern 1*a* may represent the effect of a group of peptides which help the organism to overcome metabolic blocks but which, through being present in sub-minimal amounts, fail to show sustained activity. Pattern 1*b* may represent the effect of a group of peptides which are not of themselves active but which give rise to active substances as a result of structural modifications arising through the action of enzymes produced by the bacterium. The long lag may then be regarded as the period required for the synthesis or action of the appropriate enzyme system. Alternatively, the lag may represent the interval necessary for the micro-organism to elaborate the system for transporting the peptides across the cell wall. These and other related problems are at present under investigation.

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Biosynthesis of Choline *in vitro* by Rat Liver

In conformity with the observation that only one of the three methyl groups of choline, after oxidation to betaine, can be transferred to homocysteine[1], it was shown from *in vivo* studies[2] that only the conversion of dimethylethanolamine to choline is a transmethylation, the influence of folic acid being confined to steps leading to the formation of monomethylethanolamine and dimethylethanolamine from ethanolamine. The present *in vitro* experiments were carried out to ascertain, more directly, the origin of the methyl groups of choline, and their relationship to folic acid.

Since homogenation resulted in complete loss of ability to form choline[3], several rat liver slices were incubated, separately, with ethanolamine, monomethylethanolamine and dimethylethanolamine in presence of (3-^{14}C) serine or (Me-^{14}C) methionine. The involvement of folic acid in one or more of the methylations in choline biosynthesis from ethanolamine, can be inferred from the significantly lower incorporation of activity into phosphatidyl choline by liver slices of folic acid-deficient rats as compared with those of the folic acid-supplemented controls, except when dimethylethanolamine and (Me-^{14}C) methionine were incubated together (Table 1). This lack of effect in the latter case would suggest that the methylation of dimethylethanolamine is predominantly a transmethylation. On the other hand, the appreciable amounts of activity incorporated from the methyl group of methionine into phosphatidyl choline in presence of ethanolamine and monomethylethanolamine, even in folic acid deficiency (Table 1),

Table 1. Folic Acid Deficiency and Incorporation of (Me-^{14}C)-Methionine and (3-^{14}C)Serine into Phosphatidyl Choline

Additions	(Me-^{14}C)methionine		(3-^{14}C)serine	
	+ Folic acid	− Folic acid	+ Folic acid	− Folic acid
	Total counts/min./vessel in phosphatidyl choline*			
Ethanolamine	1,452	502	1,043	268
Monomethylethanolamine	1,133	392	616	115
Dimethylethanolamine	1,918	1,486	906	172

* Average values for five independent incubations.

Each incubation vessel contained 500 mgm. of normal or folic acid deficient (ref. 4) rat liver slices in 5 ml. Krebs–Ringer phosphate buffer pH 7·4, containing 3×10^{-4} *M* (Me-^{14}C)methionine or (3-^{14}C)-serine and $3{\cdot}8 \times 10^{-4}$ *M* either ethanolamine, mono- or dimethylethanolamine. Incubations were performed in air for 2 hr. at 37° C.

The reaction was stopped by addition of 2 ml. of a 3 : 1 mixture of ethyl alcohol–ethyl ether. Extraction of phospholipids, hydrolysis and separation of choline were according to Pilgeram *et al.*, ref. 3.

would indicate that transmethylation is also involved in providing methyl groups for dimethylethanolamine synthesis. The methyl groups of choline, therefore, seem to be derived by transmethylation as well as folic acid-dependent reactions, the latter being predominant with the first two steps and the former with the last one. These observations are in keeping with recent findings of Venkataraman and Greenberg[5], who have defined an active soluble enzyme system in liver, capable of synthesizing all the choline methyl groups from formaldehyde, tetrahydropteroylglutamic acid serving as a co-factor, and of Bremer and Greenberg[6], who have shown that rat liver microsomes could synthesize monomethylethanolamine and dimethylethanolamine, as well as choline, by transmethylation.

There is a graded decrease in the activity of phosphatidyl choline formed in presence of ethanolamine and monomethylethanolamine, possibly because, on an equimolar and random basis, for every ethanolamine and monomethylethanolamine molecule, there will be 3 and 2 methyl groups respectively entering. The rate-limiting nature of earlier methylations[6] would explain the higher incorporation with dimethylethanolamine (Table 1).

Experiments in Table 2 serve to show that the observed folic acid-dependent incorporation of the β-C of serine into phosphatidyl choline, synthesized from dimethylethanolamine (Table 1) probably occurs through prior conversion to the methyl moiety of methionine[6]. The β-C of serine is incorporated more extensively into methionine than into choline of the acid-soluble fraction. The incorporation reaches a maximum in 0·5 hr., while it increases steadily for 2 hr. in phosphatidyl choline. Arnstein and Neuberger[8] have also indicated from *in vivo* work that methionine synthesis precedes choline synthesis, the hydroxymethyl group of serine being an important precursor of the methyl group of methionine.

Table 2. Relative Rates for Incorporation of (3-^{14}C)Serine into Acid-soluble Methionine, Choline and Phosphatidyl Choline

Incubation time (hr.)	Acid-soluble fraction				Phosphatidyl choline	
	Methionine		Choline			
	A	*B*	*A*	*B*	*A*	*B*
	Total counts/min./vessel*					
0	489	450	234	228	0	0
½	18,237	5,408	1,736	2,440	381	478
1	13,469	15,016	913	1,902	927	1,202
2	10,263	14,720	551	1,608	1,228	1,287
3	8,998	10,124	378	750	1,278	1,306

* Average values for five different incubations.

Each reaction vessel contained 400 mgm. rat liver slices in 5 ml. of Krebs–Ringer phosphate buffer, pH 7·4, containing 3×10^{-4} *M* (3-^{14}C)serine and $3{\cdot}8 \times 10^{-4}$ *M* each of ethanolamine and homocysteine in experiments *A* and dimethylethanolamine and homocysteine in experiments *B*. Incubations were performed in air at 37° C.

The reactions were stopped at different time intervals by adding trichloracetic acid (5 per cent). Choline, methionine and serine were added, each at 1-mgm. level, as carrier and the amino-acids separated essentially according to the method of Moore and Stein (ref. 7). Choline was eluted finally by 1·5 *N* hydrochloric acid. Phosphatidyl choline was isolated as explained in legend for Table 1.

This investigation is being extended with the subfractions of the cell.

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Reaction of Digitalis Compounds with Antimony Pentachloride

Antimony pentachloride has been used as an agent for the detection of steroids in paper chromatography by a number of investigators[1–4]. It has been found that antimony pentachloride is a useful agent for detecting certain digitalis compounds (digoxin, digitoxin and digitoxigenin) on paper chromatograms.

Crystalline digitoxin and digitoxigenin (obtained from Nutritional Biochemicals Corp., Cleveland, Ohio) in chloroform and crystalline digoxin (obtained from Burroughs Wellcome and Co., Inc., Tuckahoe, New York) in a 1 : 1 solution of 95 per cent ethanol and chloroform were placed on a 0·8 cm.[2] area on Whatman No. 7 paper in varying amounts. Antimony pentachloride in chloroform (20 gm. in 100 ml.) was sprayed on the paper. An immediate reaction occurred. All three compounds became yellow in colour and the digoxin and digitoxin quickly took on an intense purple colour. The digitoxigenin slowly took on a green colour at the 50- and 25-μgm. level, but remained yellow with lesser amounts.

Table 1. Reaction of Digitalis Compounds with Antimony Pentachloride

Compound	Colour before heating	Minimum amount detectable (μgm.)	Colour after heating	Minimum amount detectable (μgm.)
Digoxin	Purple	1·0	Black	0·5
Digitoxin	Purple	1·0	Black	0·5
Digitoxigenin	Green or yellow	1·0	Darker green or yellow	0·5

After heating the sprayed paper at 84° C. for 5–10 min. the digoxin and digitoxin became intensely black, while the digitoxigenin turned a darker shade of green or yellow.

Table 1 shows the changes in colour before and after heating and the least amount detectable. After heating the compounds were much more easily visible at the 1·0–5·0 μgm. range than before heating.

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RADIOBIOLOGY

A General Method for the Quantitation of Immune Cytolysis

THE cytolytic effect of immune serum has been the subject of study by a number of investigators. It has been shown[1] that cells other than erythrocytes undergo lytic changes in the presence of antibody and complement. It has been further shown[2], using cells labelled with phosphorus-32, that the lysis of such cells is accompanied by a release of intracellular proteins, similar to the release of hæmoglobin from lysed erythrocytes. It appeared that the immune lysis of tissue cells is quite analogous to the immune lysis of erythrocytes. On this basis, a test was developed using radioactive labelled cells which provides a means of quantitating immune lysis for cells derived from a variety of tissues.

Mouse Ehrlich ascites tumour cells grown in *CF* No. 1 female mice and the corresponding immune rabbit serum were used for the demonstration of this method. The tumour cells were collected from the peritoneal cavity of the mouse, washed 3–5 times by centrifugation and decantation with a diluent composed of veronal buffered saline, *p*H 7·4 (ref. 3), containing 1 per cent bovine albumin (Armour Laboratory, Kankakee, Illinois). The washed tumour cells were labelled with 50 μc. of chromium-51 ('Rachromate', Abbott Laboratory, North Chicago) per ml. packed tumour cells. After an incubation period of 1 hr. at room temperature, the labelled cells were washed five times with diluent. An uptake of 60–70 per cent of the radioactivity was obtained. The cell concentration was then adjusted to 1 per cent on the basis of either packed cell volume or cell count. It was found that a 1 per cent suspension corresponding to 4×10^6 cells/ml. was optimal for these tests. It was also found that only those cells were suitable which had been collected and labelled on the same day the test was performed.

The total volume of the cytolytic test was 3·0 ml., consisting of 1·0 ml. serum dilution, 1·0 ml. complement dilution (lyophilized guinea pig serum, Sharp and Dohme, Philadelphia) and 1·0 ml. of the chromium-51-labelled cell suspension. (A protocol for a typical antibody cytolytic titration is given in Table 1.) The test was incubated for 1 hr. at 37° C. and centrifuged. Then the clear supernatant fluids were gently removed by aspiration. Finally, 1·0-ml. aliquots of the supernatant liquids were counted for radioactivity. The values obtained (antibody or complement titration) were corrected for non-specific loss of radioactivity from the cells (tube 7*c* of Table 1) and then the percentage of specific lysis was calculated by dividing the corrected counts by the number of counts corresponding to 100 per cent lysis.

In order to obtain a 100 per cent value for cell lysis, it was necessary, because insoluble as well as soluble components of the cell had been labelled, to determine the amount of radioactivity associated with the soluble components only. Ultrasonic vibration was considered to be the most suitable method for cell disruption; therefore, an aliquot of the labelled cell suspension was sonated for 15 min. (magnetostriction oscillator, model *S*-102*A*, Raytheon Mfg. Co., Waltham, Mass.) and the lysed cell suspension centrifuged for 1 hr. at 16,000*g*. The clear supernatant fluid was diluted 1 : 3, and a 1·0-ml. aliquot used for counting. The counts were corrected for non-specific loss of radioactivity and were used as the value for 100 per cent lysis. This value agreed well with the number of counts found when excess complement and antibody were used to obtain maximum lysis. The values for 100 per cent lysis varied between 71 and 76 per cent of the corrected total radioactivity present.

All further treatment of the data was the same as that described by Kabat and Mayer[4] for the determination of hæmolysin titre in terms of 50 per cent hæmolytic units. The values obtained for percentage lysis (Y) of different amounts of serum or complement were converted to $Y/(1-Y)$ values and the amount of serum versus the corresponding $Y/(1-Y)$ values was plotted on logarithmic paper. The amount of serum required for 50 per cent lysis was estimated from the graph (where $Y/(1-Y) = 1{\cdot}0$). Repeated titrations of the same serum, carried out on different days, were found to agree within 5 per cent.

Table 1. TYPICAL PROTOCOL FOR THE QUANTITATION OF ANTIBODY CYTOLYTIC ACTIVITY

Tube No.	Ml. serum*	Ml. diluent (alb.-V.B.)	Ml. complement (four 50 per cent units)	Ml. 1 per cent cells (^{51}Cr labelled)	Counts/min./ 1·0 ml. aliquot supernatant	Corrected counts (−7*c*)	Per cent lysis (Y)	$\frac{Y}{1-Y}$
1	1·0	—	1·0	1·0	10,749	8,657	77	3·35
2	0·8	0·2	1·0	1·0	9,735	7,643	68	2·13
3	0·6	0·4	1·0	1·0	6,835	4,743	42	0·724
4	0·5	0·5	1·0	1·0	4,418	2,326	21	0·266
5	0·4	0·6	1·0	1·0	2,982	890	8	0·087
6	0·3	0·7	1·0	1·0	2,424	332	3	0·031
7*c*	—	1·0	1·0	1·0	2,092	—	—	—
†8*c*	—	2·0	—	1·0	17,117	15,025	—	—
‡9*c*	—	2·0	—	1·0	13,282	11,190	—	—

* Initial dilution of serum 1 : 480. † Not centrifuged, total number of counts. ‡ Supernatant from sonated cells, value for 100 per cent lysis.

Antiserum titrations were carried out in the presence of four 50 per cent units of complement. The complement titrations were carried out using optimally sensitized cells[2]. In this particular system, it was found that complement had from twenty-five to thirty 50 per cent cytolytic units per ml. All the components of this system were checked for anti-complementary activity in the sheep cell hæmolytic system and were not found to be anticomplementary in the concentrations used.

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Protective Effect of orally administered S,ß-Aminoethylisothiuronium.Br.HBr against X-radiation Death in Mice

S,ß-Aminoethylisothiuronium.Br.HBr (AET) is of known value in mice, and given parenterally in an appropriate dose will convert a $LD_{100/30}$ dose of whole-body X-radiation to essentially a $LD_{0/30}$ (ref. 1). The oral administration of AET prior to X-radiation is said to be effective (ref. 2 and Doherty, D. G., personal communication), but no definite results have yet been published. Oral cysteamine has been reported to be effective in both mice and rats with a longer duration of action than intraperitoneal injection[3], but this has been disputed[4].

The outstanding advantage of the oral use of any chemical is, of course, ease of administration. The purpose of this communication is to present data on the oral administration of AET to mice, its toxicity, its value and its duration of action.

Young adult female mice, Walter Reed Bagg strain, weighing 22–26 gm. were used in this work. The AET used was dissolved in a phosphate buffer of *p*H 7·2. The *p*H was then adjusted to 7–7·5 by the addition of the necessary amount of concentrated sodium hydroxide. The final concentration of AET was always about 100 mgm./c.c. based on the weight of the di-bromide salt. All solutions were prepared just before using.

Experimental animals were given 1,500 mgm./kgm. AET by gastric catheter (volume about 0·3 c.c.) while controls were given the same amount of the buffer solution alone.

At various times after AET administration exposure to 770 r. of whole-body X-radiation was carried out. Each exposure group consisted of experimental and control animals, totalling 20–30 mice. After exposure each group was housed in the same large cage, with standard laboratory food and water always available. Mortality and body-weight of the survivors were determined daily for 30 days.

The source of X-ray was a 250 Maxitron, operating at 250 kVp., 30 m.amp. Inherent filtration was equal to 3·2 mm. beryllium and half-value layer of 1·0 mm. aluminium and 1·0 mm. copper was added. The dose was measured in air in the appropriate mid-position of the animals with a Victoreen chamber. The rate of X-radiation was about 30 r./min. and the target source distance was 70 cm.

Toxicity analysis revealed that doses of AET of 1,200 mgm./kgm. or less were non-lethal to these mice. At 1,500 mgm./kgm. there was a 20 per cent mortality in the next 24 hr. Such a result was also noted in the treated X-radiated animals ; however, all such deaths were discarded from the experimental groups reported. At doses of 1,800 mgm./kgm. or greater there was 100 per cent mortality in 48 hr.

Fig. 1 presents the results of this experiment. A total of seven groups of control mice showed a remarkably similar 30-day mortality. For purposes of statistical comparison the control groups were averaged together.

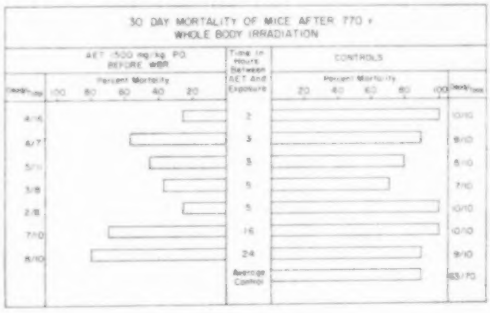

Fig. 1

AET by mouth exerts a significant protective effect at 2, 3 and 5 hr. after ingestion, but this is lost at 16 and 24 hr. Chi-square analysis of the 2 hr., 3 hr. (combined) and 5 hr. (combined) gives a $P > 0{\cdot}001$ when compared with the control $LD_{90/30}$ in a total of 70 mice. The protection achieved is not so dramatic as when AET is given parenterally.

The loss of body-weight following X-radiation was similar in all groups for the first week. Thereafter, the controls continued to lose weight and eventually died, while the AET-treated mice began to regain weight and by 30 days had generally exceeded their pre-X-radiation body-weight.

AET is as effective at 5 hr. as at 2 hr. after ingestion. Duration of the protective action is unknown, but it is not apparent at 16 hr. Nor is the earliest time for protection following oral administration known from this experiment, except that it exerts its effect at least within 2 hr. Other reports indicate that protective action is apparent within a few minutes of ingestion for AET[2] and cysteamine[4].

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PHYSIOLOGY

Repetitive Hyperpolarizing Response of the Nerve Fibre of Crayfish

THE electrical properties of the myelinated nerve fibre in potassium-rich solution were observed by Stämpfli[1], Mueller[2] and Tasaki[3]. Those of the unmyelinated nerve fibre were observed by Segal[4], Tasaki[3] and Moore[5]. When the membrane potential is depolarized by potassium, the potential difference across the membrane produced by the inward current pulse is larger than that produced by the outward one and exhibits a kind of discontinuous increase at a certain current intensity (the current-potential relation is non-linear). The time-course of the potential difference produced by the inward current has two steps. This phenomenon is called 'anodal threshold phenomenon' by Segal[4] and 'hyperpolarizing response' by Tasaki[3]. Tasaki reported that the hyperpolarizing response in the giant axon of the squid was slightly different from that in the myelinated nerve fibre.

In the present work similar experiments were made on the single motor axon (fast closer) in the claw of the crayfish (*Procambarus clarkii*), which was smaller than the giant axon of squid and was 30–50μ in diameter. Our results accorded approximately with those obtained in the nerve fibre of other animals. Responses obtained in the crayfish giant axon sometimes resembled the hyperpolarizing response obtained in the node of Ranvier of the myelinated nerve fibre and sometimes resembled that in the squid giant axon. Besides, they often appeared in the form of repetitive responses which were not observed in the other animals.

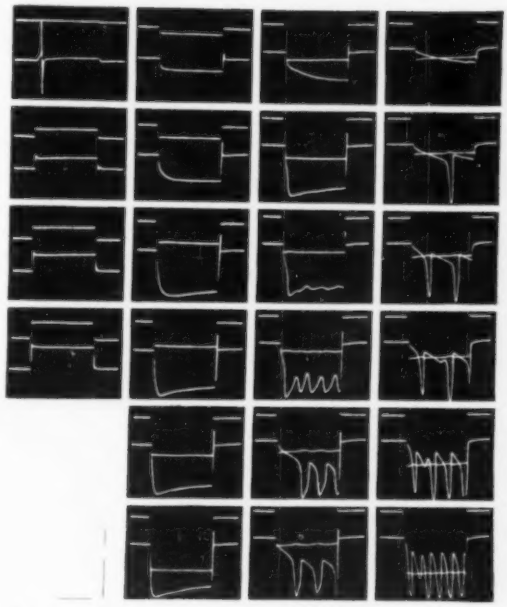

Fig. 2. Simultaneous recording of the membrane current (upper trace) and the membrane potential (lower trace) in a crayfish nerve fibre treated with potassium chloride. The concentration of potassium was increased in the order from left to right. The calibrating bar for current (upper) is 10^{-2} amp., for voltage (lower) is 50 mV. and for time is 30 msec.

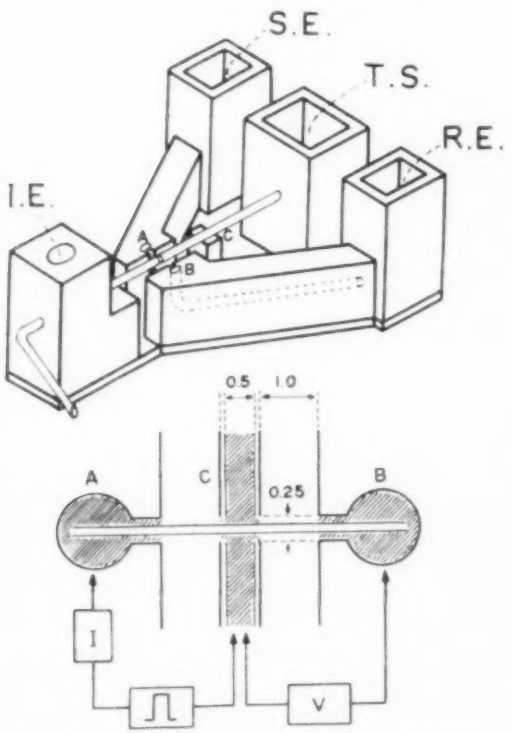

Fig. 1. Arrangement used for recording the membrane potential variation in the crayfish unmyelinated nerve fibre. The portions of the axon in pools *A* and *B* were narcotized with 0·2 per cent cocaine solution. Each pool was insulated with mineral oil

A single nerve fibre was mounted in the chamber with three pools as shown in Fig. 1. The stimulators were connected with *A*-pool and *C*-pool and the potential difference between *C*-pool and *B*-pool was recorded. *C*-pool was irrigated with the test solution. The amount of potassium ions in the medium was altered by mixing isotonic potassium chloride solution with van Harreveld solution. Sodium was replaced with potassium, while chloride, calcium and magnesium were kept normal. The portions of the axon in *A*-pool and *B*-pool were narcotized with a 0·2 per cent cocaine solution. Each pool was insulated with mineral oil.

Fig. 2 shows the potential which was produced across the membrane depolarized by potassium when a square current pulse of 50 msec. was applied. In Fig. 2, the upper trace of each photograph shows the applied current and the lower trace shows the potential produced. The concentration of sodium ion was decreased and that of potassium was increased in the order from left to right. The repetitive hyperpolarizing response was observed in the potassium-rich media (the third and fourth columns of Fig. 2). Such response could be produced no matter whether the solution contained a small quantity of sodium or not. The response resembled the ordinary action potential in several respects and had the all-or-none character with a clear threshold, displaying a critical hyperpolarization. As the concentration of potassium was increased, this response became sharper and larger. The amplitude and the duration of the response in isotonic potassium chloride solution were about 80 mV. and about 5 msec. respectively. As

the stimulus current was increased, the latency became shorter. The frequency of the repetitive response became higher on increasing the inward current. The repetitive response could last for more than 10 sec., and, when it ceased, the membrane potential reached the potential level lower than the peak of the response by about 20 mV.

The membrane in the potassium-rich media shows the same voltage-current characteristics as the semiconductor. The repetitive response may be produced by a negative resistance property of the membrane as known from semiconductor theory. In other words, the factor which causes the repetitive response may be explained by the spontaneous change between the two stable states of the potassium permeability, one of which is the increased state and the other of which is the decreased state[1,3,4,5].

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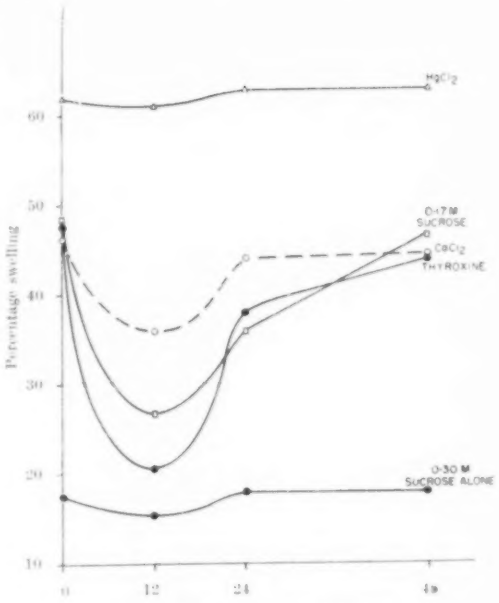

Fig. 1. Effect of intraperitoneally injected liver mitochondria obtained from partially hepatectomized rats on the hepatic mitochondrial swelling of the host rats. The test systems for mitochondrial swelling were 1×10^{-5} *M* thyroxine or mercuric chloride, or 5×10^{-3} *M* calcium chloride in 0·30 *M*, *p*H 7·4 sucrose, or 0·17 *M*, *p*H 7·4 sucrose alone. Each point on the curves corresponds to the swelling at 40 min.

Transmission of Swelling Characteristics by Mitochondria of Regenerating Liver

As an outcome of previous work on the fine structural changes of cell particles during induced hepatic carcinogenesis[1-3] and rapid liver growth[3], it has been found that the mitochondria isolated from regenerating rat liver transmit their swelling characteristics to the hepatic mitochondria of the host rats following intraperitoneal injection.

Male Sprague–Dawley rats (average 280 gm.), fed 'Purina chow', were used. The animals were killed 12 hr. after partial hepatectomy, where two-thirds of the liver was removed under light ether anæsthesia. The mitochondrial fractions isolated as described[2] from two animals were pooled, suspended in 3 ml. 0·25 *M* sucrose, and injected intraperitoneally to rats. The controls were injected with mitochondria from intact, non-hepatectomized rats. For the preparation of the mitochondrial membrane (crista) and intra-cristal protein fractions, the mitochondria from two partially hepatectomized rats were pooled, and suspended in 5·5 ml. of distilled water that contained, per litre, 1 ml. of a phosphate buffer (411 gm. dipotassium hydrogen phosphate + 163 gm. potassium dihydrogen phosphate per litre). The suspension was incubated for 40 min., then centrifuged for 12 min. at 25,000*g*. The sedimented membrane fraction was resuspended in 3 ml. of 0·9 per cent sodium chloride solution, while a concentrated sodium chloride solution was added to the decanted supernatant to bring the final concentration of sodium chloride to 0·9 per cent. Both fractions were injected intraperitoneally to separate animals. The swelling of the liver mitochondria of the injected animals was measured at the time-intervals shown in Fig. 1, by the optical density method as described previously[2]. All experiments were carried out in triplicate.

In contrast to the results shown in Fig. 1, the mitochondria isolated from the control rats, which were injected with liver mitochondria from intact, non-hepatectomized animals, exhibited no, or only very slight, change in swelling. In the experiments with the isolated membrane and intra-cristal protein fractions corresponding alterations in mitochondrial swelling were observed in the thyroxine and calcium chloride test systems when the rats were injected with the membrane fraction. However, unlike whole mitochondria, injection of this fraction did not produce changes in the swelling induced by 0·17 *M* sucrose. The intra-cristal protein fraction did not produce noticeable changes in swelling with either of the test systems used.

That rapid tissue growth is associated with low levels of mitochondrial swelling has been shown previously with rat hepatoma[2-4], and with rat liver following partial hepatectomy or intraperitoneal injection of 20-methylcholanthrene[3]. In view of these results, the transmissible decrease of mitochondrial swelling, produced by mitochondria of regenerating liver, found by us correlates with the stimulation of hepatic mitotic rate by injected whole homogenates of rapidly growing tissues[5,6] or isolated microsomes and mitochondria from rapidly dividing cells[7]. Since tissue growth is associated with enhanced rate of protein synthesis which is in turn dependent on the rate of production of adenosine triphosphate, it is not unexpected that growth affects the mitochondrial membrane site of intense oxidative phosphorylation and thus, the characteristics of

swelling. Hence, further evidence is provided in support of the correlation between rapid tissue growth and low values of mitochondrial swelling[2,3]. A more detailed study of the reported phenomenon is in progress.

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Incorporation of Ethanol-1-^{14}C into Fatty Acids in the Normal and Alloxan Diabetic Rat

RECENT work in this laboratory has shown that, in the mouse, ethanol-1-^{14}C is incorporated *in vivo* into phospholipids, cholesterol, and fatty acids at approximately the same rate and to the same degree as acetate-1-^{14}C (ref. 1). It is well known that in diabetic animals a metabolic block exists in the synthesis of fatty acids from acetate[2]. It was of interest to determine whether ethanol can be used to any greater degree as a source of building blocks for fatty acid synthesis in diabetic animals, or whether a similar metabolic block occurs.

Long-Evans rats of 250–350 gm. maintained on Wayne laboratory chow were used. Alloxan diabetes in rats was produced by the subcutaneous injection of 150 mgm. alloxan per kgm. in citric acid buffer according to Klebanoff and Greenbaum[3]. Rats were considered diabetic when urine sugar was greater than 250 mgm. per cent two weeks after injection of alloxan. Acetate-1-^{14}C and ethanol-1-^{14}C were obtained from Nuclear-Chicago. Solutions of radioactive acetate and ethanol were measured by means of a Packard Tri-Carb scintillation counter.

The incubation medium consisted of 2 or 4 μc. of ethanol-1-^{14}C or acetate-1-^{14}C diluted with 170 μM of the non-radioactive compound in 4 ml. 0·1 M phosphate buffer, *p*H 7·4. Approximately 500 mgm. of liver slices cut by means of a Stadie-Riggs tissue slicer were inserted into 25-ml. Erlenmeyer flasks containing the incubation medium, the flasks were gassed with pure oxygen and incubated for 2 hr. at 37°. At the end of the incubation time the medium was decanted on filter paper and the total lipids in the slices were isolated by the method of Baruch and Chaikoff[4]. The chloroform solutions of lipids were plated on copper planchets and the radioactivity was determined in a Nuclear-Chicago gas-flow counter using the end window.

In agreement with my *in vivo* work in mice, rat liver slices incorporate ethanol and acetate into liver lipids at approximately equal rates and to the same degree (Table 1). In diabetic animals ethanol and acetate incorporation was severely and equally depressed. In the diabetic rats, the rate of ethanol incorporation into liver lipids was 22 per cent of normal, while acetate incorporation was 17 per cent of normal. This small difference in incorporation is not considered significant. The fact that the liver slices from the diabetic animal were able to utilize ethanol and acetate to approximately the same extent in their slow rate of lipid synthesis indicates that the diabetic animal is able to convert ethanol to acetate at an adequate rate and that the metabolic block must occur beyond this point. Recent work elsewhere[5] has suggested that ethanol and acetate do not participate equally in fat metabolism. We infer from these experiments, however, that ethanol and acetate are equivalent as a source of liver lipid synthesis both *in vivo* and *in vitro*.

Table 1. INCORPORATION OF ETHANOL-1-^{14}C AND SODIUM ACETATE-1-^{14}C INTO LIVER LIPIDS IN NORMAL AND DIABETIC RATS

	Ethanol-1-^{14}C c.p.m./gm. liver slice	Acetate-1-^{14}C c.p.m./gm. liver slice
Normal (average of 12 animals)	1,111 ± 90	1,033 ± 148
Alloxan diabetic (average of 6 animals)	251 ± 49	176 ± 61

The incubation flasks contained 170 μM (2 μc.) of the radioactive compound in 4 ml. 0·1 M phosphate buffer *p*H 7·5. Incubation time was 2 hr.

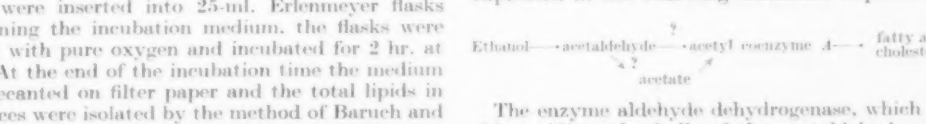
When normal liver slices are presented with either ethanol or acetate as a source of lipid building blocks, acetate is the preferred substrate. Isotopic competition studies show that equimolar amounts of non-radioactive acetate inhibited the incorporation of radioactive ethanol into lipids 75 per cent (Table 2). On the other hand, non-radioactive ethanol did not depress entrance of acetate-1-^{14}C into the lipid-building metabolic sequence more than about 10 per cent. Table 2 also shows that in alloxan diabetic animals a parallel relationship exists.

Table 2. INCORPORATION OF ETHANOL-1-^{14}C AND SODIUM ACETATE-1-^{14}C INTO LIVER LIPIDS ALONE AND IN THE PRESENCE OF EQUIMOLAR AMOUNTS OF NON-RADIOACTIVE ACETATE AND ETHANOL RESPECTIVELY

	Ethanol-1-^{14}C c.p.m./gm. liver slices	Ethanol-1-^{14}C + acetate c.p.m./gm. liver slices	Acetate-1-^{14}C c.p.m./gm. liver slices	Acetate-1-^{14}C + ethanol c.p.m./gm. liver slices
Normal (average of 3 animals)	2,294 ± 480	710 ± 142	1,947 ± 318	1,752 ± 216
Alloxan diabetic (average of 3 animals)	378 ± 16	80 ± 25	227 ± 106	201 ± 21

Conditions are as described for Table 1 except that the medium contained 4 μc. of the radioactive compound and the incubation time was 3 hr.

Whether ethanol and its oxidation product, acetaldehyde, enter the acetate pool as acetate *per se* or directly as an activated 2-carbon fragment has not yet been definitely settled. These alternatives are expressed in the following metabolic sequence:



The enzyme aldehyde dehydrogenase, which probably oxidizes the bulk of the acetaldehyde, yields acetate as the product[6]. My results suggest that ethanol follows the metabolic sequence: acetaldehyde → acetate → activated acetate, since ethanol

incorporation into lipids is depressed by additional acetate, while non-radioactive ethanol dilutes the radioactive acetate incorporation not more than 10 per cent. If acetaldehyde were directly converted to acetyl coenzyme *A*, a reciprocal dilution effect between the two radioactive precursors should be observed. It is not likely that the presence of acetate is inhibiting the oxidation of acetaldehyde since this reaction is known to be irreversible. Furthermore, I have shown that acetate does not slow the rate of ethanol oxidation[7]. My results best fit the theory that acetaldehyde from ethanol is converted to free acetate before entering the metabolic pool.

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Effect of Splenectomy on the Resistance of Rats to Histamine Stress

THE spleen has been suggested by many investigators as a site of production of hormones or hormone-like substances; interrelationships have been postulated with the pituitary, adrenal, gonad and thyroid glands. The present communication on the relationship of histamine tolerance to splenectomy provides additional evidence for a splenic humoral contribution.

Two hundred and ten female Wistar rats averaging 75 gm. were matched by weight and divided into three groups (*A*, *B* and *C*) representing respectively splenectomized rats, sham-operated animals and normal controls. The splenectomies were completed under open-ether anæsthesia, as described by Farris and Griffith[1]. The splenic pedicle was ligated and cut as close to the hilus as possible. The incisions were closed in two layers, surgical gut being used for the abdominal wall, and silk for the skin surfaces. Sham-operated females were subjected to the same operative procedures except for the surgical removal of the spleen. After four weeks, 60 animals in each group were selected and equal numbers tested for histamine resistance. The histamine challenge was at four dose-levels, 450, 600, 750, 900 mgm./kgm. of body-weight. Identical procedures were utilized for male animals. Finney's method of probit analysis was used to calculate the LD_{50} values and dose-response lines[2].

Table 1 presents the results. Comparisons between the LD_{50} values for groups *A* and *B* indicate that splenectomy induced 5·1 per cent increase in the tolerance of female and 14·9 per cent increase in the tolerance of male rats to histamine stress. In the males, the increase approached statistical significance ($P = 0{\cdot}13$). In no instance did any of the differences between the sham and unoperated controls attain or approach statistical significance. It is of interest that the increase in tolerance observed in the male was greater than the comparable increase in female rats. This finding suggests the possible existence of a sex difference in splenic function, a suggestion supported by previous reports of sex differences in response to histamine in parathyroidectomized[3] and thymectomized[4] animals.

Table 1. EFFECTS OF SPLENECTOMY ON THE LD_{50} VALUES OF MALE AND FEMALE RATS

	Group *A*: splenectomized rats	Group *B*: sham-operated rats	Group *C*: normal control rats
I. *Male* LD_{50} (mgm./kgm. ± S.E.)	754·3 ± 68·2	656·6 ± 63·4	686·6 ± 56·7
Percentage difference between LD_{50} values	*A* : *B* + 14·9 per cent *A* : *C* + 9·9 per cent	*B* : *C* − 4·4 per cent	
P values	*A* : *B*, 0·13 *A* : *C*, 0·30	*B* : *C*, 0·64	
II. *Female* LD_{50} (mgm./kgm. ± S.E.)	703·8 ± 49·9	669·6 ± 54·1	661·1 ± 55·7
Percentage difference between LD_{50} values	*A* : *B* + 5·1 per cent *A* : *C* + 6·5 per cent	*B* : *C* + 1·3 per cent	
P values	*A* : *B*, 0·48 *A* : *C*, 0·38	*B* : *C*, 0·88	

A : *B*, results of comparisons between results for group *A* and group *B*, *A* : *C*, group *A* and group *C*, and *B* : *C*, group *B* and group *C*, respectively.

That splenectomy tends to increase tolerance to histamine stress is in accord with the protective action against epinephrine-induced pulmonary œdema[5] and toxic doses of 2-thio-5-methyl-uracil[6] induced by splenectomy.

Although the investigation does not offer conclusive evidence concerning a splenic endocrine function, the results provide inferential support for such a hypothesis.

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An Effect of Chlorpromazine on Rat Mitochondrial Membranes

THE phenothiazines used in therapy appear to affect membranes in many biological systems. Thus, Greig *et al.*[1], among others, have shown that promethazine, a phenothiazine type of antihistaminic drug, prevents the usual deterioration of red blood cells during storage. This presumably is a membrane effect. The frog gastrocnemius muscle swells when placed in distilled water. This water imbibition can be partially prevented by chlorpromazine[2]. A few *in vivo* experiments may be cited as well. Thus,

the metrazol-enhanced passage of dyes into the brain is antagonized by chlorpromazine[3]; the absorption of sugar from the intestine[4] and drugs from subcutaneous depots[5] are both retarded by chlorpromazine. Close inspection of the entire literature dealing with the actions of chlorpromazine on all types of biological systems revealed that most of the test systems employed contained semipermeable membranes of one type or another (cellular or sub-cellular). For this reason the possibility should be considered that these structures are the primary loci of attack by the drug, while the numerous other reported effects may be secondary.

Prominent among the membranes thought to be affected by chlorpromazine are those of the mitochondrion[6–8]. Roizin *et al.*[8] have presented preliminary evidence that pretreatment of rats with this drug caused changes in the size and structure of brain mitochondria. Bernsohn *et al.*[9] believed that the inhibitory effect of chlorpromazine on the enzyme hexokinase present in rat brain homogenate was an indirect one, since they were unable to demonstrate inhibition of a purified yeast hexokinase with this drug. However, no experiments with the non-particulate mammalian enzyme were performed. Although it is true that in a few isolated instances chlorpromazine does inhibit non-particulate enzyme preparations directly, this does not negate the possibility that the pharmacologically important action of this drug is concerned with changes in biological membranes. Finally, it must be considered that chlorpromazine membrane effects, such as slowing or preventing substrate uptake, or changing enzyme leakage from mitochondria, for example, could mistakenly be interpreted as an inhibition of a particular enzyme under observation.

Since a majority of the papers scrutinized employed either isolated mitochondria or tissue preparations containing mitochondria, an investigation of the effect of chlorpromazine on the permeability of these organelles to water or water-soluble ions was undertaken. It is known that the optical density of a suspension of mitochondria in an aqueous medium is a function of their volume[10]. Swelling results in a lowering of optical density which can easily be followed spectrophotometrically at the arbitrary wave-length of 520 mμ. Such swelling can be induced in both brain and liver mitochondria from Wistar rats by a variety of means, including osmotic dilution, phosphate ions plus osmotic dilution, thyroxin and many detergents, including 'Triton *X*-100'. The effect of chlorpromazine on these different types of mitochondrial swelling is shown in Table 1. Under the conditions of these experiments, chlorpromazine considerably inhibits all the types of swelling, many at low concentrations. Occasionally, effects were noted at concentrations as low as 10^{-6} *M* for brain using 'Triton' as a swelling agent, or 10^{-7} *M* for liver with thyroxin as the swelling agent. The concentrations of chlorpromazine are smaller than those generally necessary to produce changes in enzyme activities or in the level of oxidative phosphorylation.

Table 1. Inhibition of Mitochondrial Swelling by Chlorpromazine

Mitochondrial source	No. of exp.	Swelling agent	Molar concentration of chlorpromazine inhibiting mitochondrial swelling 30 per cent
Brain	6	Phosphate + water	5×10^{-4}
	15	'Triton *X*-100' + sucrose	10^{-5}
Liver	6	Water	2×10^{-4}
	6	Phosphate + water	5×10^{-5}
	20	Thyroxin + sucrose	$1{\cdot}2 \times 10^{-6}$
	6	None	5×10^{-6}*

* Prevention of endogenous swelling when mitochondria were suspended in 0·3 *M* sucrose.

Mitochondria from 50–100 mgm. of rat brain or 12–20 mgm. of rat liver suspended in 0·1–0·2 ml. of 0·25 *M* sucrose were added to 0·25–0·30 *M* sucrose, or water or 0·25 *M* phosphate buffer at *p*H 7·4. Thyroxin when added to liver mitochondria was present at a final concentration of 10^{-6} *M*; 0·44 ml. of a solution of 0·125 per cent (v/v) 'Triton *X*-100' was usually added to brain mitochondria when needed. The final volume in all cuvettes was 3·0 ml. Mitochondrial swelling caused a fall in optical density which was measured by means of a Beckman Model *DU* spectrophotometer at 520 mμ. The change in optical density was generally followed over a 10-min. period.

The concentrations of chlorpromazine are smaller than those generally necessary to produce changes in enzyme activities or in the level of oxidative phosphorylation.

These experiments therefore give some support for the idea that chlorpromazine primarily causes a change in membrane permeability.

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Effects of Chlorpromazine and Lysergic Acid Diethylamide on the Rate of Habituation of the Arousal Response

The responsiveness of an animal to sensory stimulation is dependent to a large extent on past experience as well as the precise conditions to which the animal is subjected. A continually repeated auditory stimulus presented in a stable environment gradually produces indifference whereas the association of a reward or a punishment brings about heightened attentiveness and increases the arousal value of the auditory stimulus[1]. Systemic administration of certain drugs may produce similar effects but for a wider range of stimuli. Blocking of sensory-induced electrocortical arousal and behavioural indifference characterize some of the central effects of chlorpromazine in cats[2]. On the other hand, *d*-lysergic acid diethylamide (LSD 25), administered in small doses, produces increased responsiveness to most sensory stimuli[3]. Chlorpromazine has also been shown to block conditioned avoidance behaviour and markedly decrease the ability of the animal to learn simple positive conditioned responses[4].

It may be that the effect of chlorpromazine on arousal responses and conditioned avoidance behaviour is due not to an all-or-nothing blocking of the responses but to an increased rate of negative learning or habituation. Conversely, LSD 25 may

interfere selectively with this latter process, thereby inducing increased responsiveness. The effects of these two drugs have therefore been compared on the rate of habituation of an arousal response evoked by an auditory stimulus, both in terms of the behaviour of the animal and the electrical activity of the cerebral cortex.

Experiments were carried out on five chronic cat preparations carrying permanently implanted cortical recording electrodes. For recording purposes the animals were housed in a double-walled, semi-sound-proofed cubicle fitted with a one-way observation window. Thus the behaviour of the animal could be correlated concomitantly with the electrocortical activity. An auditory stimulus of 1,000 c./sec., obtained from an audio-oscillator, was fed into a loudspeaker fitted in a side wall of the box.

The rate of habituation of the arousal response was found to be dependent on a number of factors such as the intensity, the duration and the rate of presentation of the stimulus. Thus the experimental procedure was standardized and the auditory stimulus was presented at intervals of 5–10 min., depending on whether or not the required depth of sleep was indicated in the electrocorticogram. The duration of the stimulus was kept constant at 8 sec., while the animal was always allowed a period of acclimatization in the cubicle before each experiment was started. Each animal was habituated to the auditory stimulus at a known intensity following an injection of normal saline. When habituation was complete a very loud, brief noise was suddenly presented in an attempt to dishabituate the animal. A period of 2–3 weeks then elapsed before the same procedure was repeated after the injection of the appropriate drug. The experiments were conducted therefore in a control, drug, control sequence in order that some assessment of the amount of retention of habituation from experiment to experiment could be made. The results obtained are illustrated graphically in Fig. 1 where the number of trials required to produce habituation of the electrocortical arousal response has been plotted against the intensity of the 1,000 c./sec. tone, expressed in decibels above an arbitrarily chosen reference-level (0·1 mV. into a 15-ohm impedance).

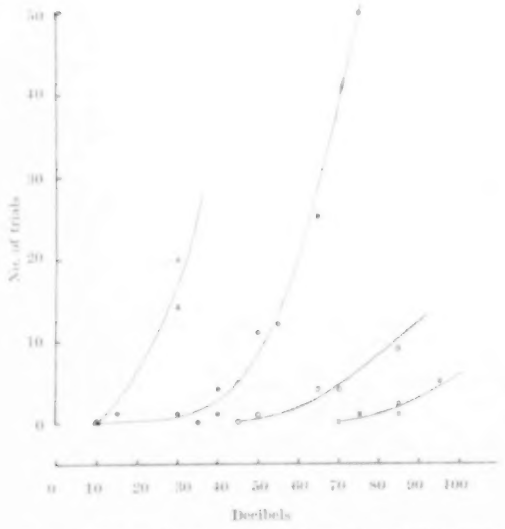

Fig. 1. Effect of chlorpromazine and *d*-lysergic acid diethylamide on the rate of habituation of the electrocortical arousal response evoked by a 1,000 c./sec. pure tone at different levels of intensity. △, 15 μgm./kgm. LSD 25; ●, control; ○, 5 mgm./kgm. chlorpromazine; ×, 10 mgm./kgm. chlorpromazine. Both drugs injected intraperitoneally

The pattern of habituation of the electrocortical arousal response was similar to that reported by Sharpless and Jasper[8]. Continued presentation of the auditory stimulus at a constant intensity brought about a progressive decrease in the period of electrocortical desynchronization until the electrical pattern of low-amplitude fast activity characteristic of the wakeful state, failed to appear. Behavioural arousal, which was indicated in the initial trials by ear movements, opening of the eyes and usually some head or body movements, or in the later stages by slight eye movements only, disappeared three to four trials before habituation of the electrocortical response.

The intraperitoneal injection of 5 mgm./kgm. or 10 mgm./kgm. of chlorpromazine was followed by an increase in the intensity of stimulation necessary to elicit the arousal response. There was also a marked increase in the rate of habituation. Where previously 45–50 presentations of the auditory stimulus had been required to produce habituation of the electrocortical arousal response, 3–4 or, with the higher dose of the drug, 1–2 trials were now sufficient to produce a similar effect using the same intensity of stimulation (Fig. 1 at 70 db.). Moreover, the period of desynchronization in the electrical record evoked by the tone before habituation took place was much shorter than in the control experiments. Behavioural arousal became habituated even more rapidly than the electrocortical response and when present in the initial trials was not very marked, being indicated by slight ear and eye movements or occasionally, at the higher intensities of stimulation, by the lifting of the head.

In contrast, following the administration of LSD 25 in doses of 10–15 μgm./kgm., intraperitoneally, the animals became increasingly responsive to all modalities of stimulation, so much so that periods of sleep activity in the electrocorticogram were very difficult to obtain. Presentation of the auditory stimulus was followed by abrupt arousal and long-lasting periods of alerting, both electrocortically and behaviourally. Thus, due either to the lack of the appropriate level of sleep activity in the electrical record or to the failure of the response to become habituated during the period when the drug was acting, it was possible to assess with some degree of accuracy the rate of habituation in only two out of a total of ten experiments with this drug (Fig. 1). These experiments demonstrated that even at low intensities of stimulation a greater number of trials was necessary before habituation occurred, indicating that the injection of LSD 25 produced a decrease in the rate of habituation.

In conclusion, it would appear that the changes in responsiveness of animals to sensory stimulation following systemic administration of LSD 25 or chlorpromazine could be brought about by the ability of these drugs to interfere selectively and antipodally with processes concerned in habituation or negative learning. The fact that there is also an increase in the intensity of auditory stimulation necessary to evoke an arousal response following chlorpromazine suggests that the effect of this drug on sensory-induced arousal is not produced solely by the increased rate of negative learning. There appears to be a decrease in the significance or meaning

attached to the novel tone by the animal after this drug is injected.

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Biological Activity of Some Humic Fractions isolated by means of Partition Chromatography

Humus has often been said to possess effects on plant growth over and above the value to plants of the plant nutrients it may release during growth.

Attempts have been made by Forsyth[1] and by Trojanowski[2] to extract humus and separate the constituents. Forsyth separated the aqueous extract of humus (fulvic acids), and Trojanowski isolated, by means of chromatography, the compounds of a group of hymatomelanic acids (ulmic acids), which have so far been little investigated. Hymatomelanic acids have now been isolated from various peats and composts using Trojanowski's method.

The crude material was freed from bituminous matter with a mixture of benzene and ethanol. Calcium and iron ions were removed by 0·2 *N* hydrochloric acid. The material was then extracted with ethanol, and the hymatomelanic acids precipitated from the ethanol extract by calcium acetate at *p*H 6·8. The precipitate was washed with 0·5 *N* hydrochloric acid and water, and then dissolved in acetone, the insoluble residue being removed by centrifuging. The acetone solution was transferred to a column of Whatman cellulose powder (30 gm. cellulose in a tube of diameter 3·5 cm.), saturated with acetone/water (20 : 1 vol.), and developed with *n*-butanol saturated with water + acetone (1 + 1 vol.). Under ultra-violet light five fluorescent bands were detected. The bands were eluted successively with acetone and water, and the eluates re-chromatographed on Whatman paper No. 1 in order to check their homogeneity. The paper chromatogram was developed with water saturated *n*-butanol/acetone/0·5 *N* hydrochloric acid (12 : 12 : 1·5 vol.). The R_F values of the spots were 0·53, 0·73, 0·95 (for fractions from low peat), and 0·45, 0·48, 0·53, 0·69, 0·95 (for fractions from compost).

The activity of the fractions was determined by the *Avena* split coleoptile test of Thimann and Schneider[3]. Controls used were: (1) re-distilled water + sodium chloride in the same quantity as used for the preparation of the solutions of hymatomelanic acid fractions, (2) indole-3-acetic acid solution (0·0025 gm./1,000 ml.), (3) solutions prepared from the ash of hymatomelanic acid fractions.

A stimulating influence on growth was found in hymatomelanic acid fractions from low peat with R_F value 0·53 and 0·95 (concentrations of 0·01 gm./100 ml.) and in fractions obtained from compost with R_F values 0·45 (concentration 0·01 gm./100 ml.), R_F 0·53 (concentrations 0·03 gm./100 ml.) and R_F 0·95 (concentration 0·09 gm./100 ml.). The stimulating influence of these fractions is similar qualitatively to that of indole-3-acetic acid. No free indole compounds were found in the fractions examined. Under these conditions unpurified complexes of hymatomelanic acids did not show any physiological activity. The observed effects could not have been caused by the mineral constituents of the humic preparations.

A possible explanation for the findings seems to be that curvatures of this type are due to inherent differences in the response to humic substances of adjacent layers of tissue.

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HÆMATOLOGY

Age and Molecular Weight of Dextrans, their Coating Effects, and their Interaction with Serum Albumin

Dextrans coat blood platelets and red cells[1] and interact with human serum albumin[2]. Recently two new problems have presented themselves. The first is that the interaction of the same sample of dextran with serum albumin appeared to be less after the dextran had been stored at 4° C. for about four years, and that the interaction of 'Synkol' (a Russian dextran of unknown age) was still less. The second is that, while the coating effects of dextrans of varying molecular weight scarcely varies, the interaction of the higher molecular weight dextrans with serum albumin has not been measured.

Effect of age of dextran on coating. Through the kindness of Dr. Norman Wheeler of the Abbott Co., we have been able to obtain two specimens of a dextran with a molecular weight similar to that of 285W3.4 of the Commercial Solvents Co. These two samples of dextran, made by the same process, had been stored for 6 and 40 months respectively, and will be referred to as 'new' and 'old' Abbott dextran. Their viscosity relative to that of saline buffered at *p*H 8 and their coating effect on human platelets and red cells are compared in Table 1 with that produced by 'old' dextran 285W3.4. The viscosities of the new and the old Abbott dextrans are virtually identical, and are about 0·97 times that of old dextran 285W3.4. The coating effects of the new and the old Abbott dextrans, determined in a vertical electrophoresis cell and expressed as U/U_0 (see ref. 1), are virtually identical, and almost the same as those of 285W3.4. The coating effects do not seem to depend

Table 1

	η/η_1	Platelets U/U_0 (per cent)	Red cells U/U_0 (per cent)
Abbott new	1·22	1·31 ± 2·7	1·09 ± 1·9
Abbott old	1·23	1·32 ± 3·1	1·09 ± 1·7
285W3.4	1·27	1·30 ± 2·4	1·09 ± 1·5

Table 2

	Mol. wt. × 10^{-3} (mean)	K_1	K_2	K_3	K_4	$-A$	$+D$	α_1	α_2	α_3	α_4
Abbott 'new'	86	44	42	45	42	4	4	0·0018	0·0013	0·0014	0·0017
Abbott 'old'	89	44	42	46	42	4	5	0·0018	0·0013	0·0014	0·0017
C.S.C. No. 6	194	59	26	34	50	8	8	0·0018	0·0008	0·0011	0·0015
C.S.C. No. 7	225	59	32	40	52	7	8	0·0018	0·0010	0·0012	0·0016
C.S.C. No. 8	412	59	33	41	51	8	8	0·0018	0·0010	0·0012	0·0016

on the time during which these dextrans have been stored, at least up to 40 months.

Effect of age of dextran on interaction with serum albumin. The interaction with serum albumin of new and old Abbott dextrans was compared by the micro-Tiselius method already described[2]. The highest concentration of serum albumin (Cohn's Fraction V, kindly supplied to us by the American Red Cross) was 2 per cent, and the highest concentration of dextran 1·5 per cent; the *p*H of the systems was 8·55, using Michaelis buffer. (The interaction of dextran 285*W3A* with serum albumin is the same between *p*H 6·6 and 9·6 in Michaelis buffered systems, and is the same at *p*H 8·6 in Michaelis and Dole buffered systems.)

The first two rows of Table 2 show the results obtained for new and old Abbott dextrans. Here K_1, K_2, K_3 and K_4 are the constants (slopes) of the four straight lines, passing through the origin, for albumin, dextran, dextran in the serum albumin–dextran mixture, and albumin in the serum albumin–dextran mixture, while α_1, α_2, α_3 and α_4 are the specific refractive increments for the same four lines. The interaction of these two Abbott dextrans with human serum albumin are substantially the same, although one had been stored for 6 months and the other for 40 months. The values $-A$ and $+D$ may indicate the extent of transfer of albumin to dextran when interaction produces a new species, but, except for saying that the formation of the new species always results in a transfer of albumin to dextran, it is not safe to be more definite.

Effect of molecular weight on interaction with serum albumin. Experiments on coating of human platelets and red cells have not shown any dependence on the molecular weight of Commercial Solvents Co. dextrans of mol. wt. 77,100–412,000 [1]. Samples of these dextrans, referred to as Nos. 6, 7 and 8, have been kept for 4 years at 4° C. in the solid state; they can each be made up as a 6 per cent solution in 1 per cent sodium chloride, dialysed against large volumes of Michaelis buffer at *p*H 8·55, and allowed to interact with 2 per cent serum albumin. This interaction is measured as already described[2].

The results are shown in rows 3, 4 and 5 of Table 2, K_1, etc., α_1, etc., and $-A$ and $+D$ having the same meaning as described for rows 1 and 2. The values suggest that there is a more extensive interaction when the molecular weight of the dextran is high, but the computations are difficult in the best of circumstances, and their reliability is lessened by the solutions of the higher dextrans being slightly opalescent; this makes the spikes slightly fuzzy, and reduces the accuracy with which the areas under them can be measured.

The coating of human red cells and platelets thus seems to be the same for dextrans of molecular weight 86,000–412,000. Low molecular weight dextrans (mol. wt. 86,000) interact to the same extent with human serum albumin whether they have been stored for 6 months or 40 months. Dextrans of high molecular weight appear to interact with human serum albumin to a greater extent than do those of low molecular weight, but the differences are small, and may be due to technical difficulties.

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PATHOLOGY

Leukæmogenesis by Urethan in New-born Swiss Mice

After earlier evidence that urethan induces or enhances the formation of pulmonary adenomas in rodents[1–3], more recent reports suggest a multipotential carcinogenic activity of this chemical. Salaman and Roe[3] and Graffi *et al.*[4] first demonstrated that urethan initiates skin carcinogenesis although it does not induce skin tumours when administered alone. Tannenbaum and Silverstone[5], by long-term application of urethan to the skin of inbred mice, observed not only lung adenomas but also tumours of the mammary gland, interscapular fat, and lacrimal glands. Kawamoto *et al.*[6] reported the augmenting influence of urethan on leukæmogenesis induced in low-leukæmic strains of mice by X-rays, œstrogenic hormone or methylcholanthrene. Berenblum and Trainin[7] showed that urethan treatment following X-irradiation results in a striking increase of leukæmogenesis in *C57BL* mice.

So far as the induction of leukæmia is concerned, the enhancing property of urethan is considered by these investigators as a 'co-leukæmogenic' effect, since it is generally accepted that urethan by itself is not leukæmogenic. The influence of urethan on leukæmogenesis, however, has not yet been studied in new-born mice, although there is good evidence that new-born animals are particularly susceptible to viral or chemical leukæmogenic agents[8,9].

In the present work new-born Swiss mice, less than 24 hr. old, were injected subcutaneously with a single dose of 0·05 ml. of a 4 per cent solution of urethan in distilled water. The Swiss mice were originally obtained from the Arsal Co., Rome. The incidence of spontaneous leukæmia in these animals, as controlled on several hundreds of old mice bred at random in this laboratory, is less than 1 per cent.

The results of the present experiment, which refer to a 6-months period of observation, were as follows: thirteen out of the 60 male and female mice given urethan at birth (an incidence of 21·6 per cent), developed malignant lymphomas between 73 and 157 days of age. The average age for onset of the disease was 107 days. All the animals showed

striking enlargement of the thymus, which filled almost completely the chest cavity. In eight mice there was also marked involvement of superficial and deep lymph nodes as well as spleen. In addition, multiple lung adenomas were observed in all cases. Histologically, the lymphomatous lesions were of the lymphoblastic-lymphocytic type. Infiltrations of heart, lungs, liver, kidneys, gonads and bone marrow were found microscopically. In the peripheral blood there was in some cases a remarkable lymphocytosis with many immature cells of the lymphoid series, although the total number of leukocytes did not show abnormalities. In a single case, however, the leukocyte count at the final stage of the disease was about 300,000 per mm.³.

From the results reported here, it would appear that urethan, *per se*, has the property of inducing leukæmia when a single dose is injected into new-born animals. The occurrence of leukæmia following the administration of an agent, such as urethan, which has been considered hitherto free from leukæmogenic activity, is probably to be regarded as dependent on factors inherent to the particular stage of development of the animals at birth[9,10].

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Influence of a Liver Fraction on the Phagocytic Activity of the Reticulo-Endothelial System in Mice

The bacterial pyrogens (lipopolysaccharides) are reported to have a marked influence on the resistance of experimental animals to bacterial challenge[1]. The reaction follows a particular pattern: during the first few hours after injection there is a drop in the resistance to infection, followed by an increase which can be quite considerable. Halpern *et al.*[2] have shown that the injection of lipopolysaccharides in mice is followed by increased phagocytic activity of the reticulo-endothelial system. On the other hand, when increased phagocytic activity is achieved by some other procedure, namely, immunization with *BCG*, the lethal effect of bacterial endotoxins is greatly enhanced[3]. The explanation for this may be found in the fact that a stimulated reticulo-endothelial system will have a greater ability to phagocytize the endotoxins without the concordant ability to neutralize their toxic effect on the organism. After finding that a particular leucocytosis-promoting liver fraction had the properties of stimulating the resistance against bacterial challenge in mice, as well as in human beings, we found it of great interest to investigate whether this fraction would have some influence on the phagocytic activity in mice.

Table 1. Effect of Liver Fractions on the Phagocytic Activity of the Reticulo-Endothelial System

	No. of animals	Phagocytic index *K*	W/WLS*	6 hr. before testing: Corrected phagocytic index
Experiment *A*: Liver fraction I 0·2 mgm./mouse				
Treated	5	0·025	16·9	4·9
Controls	5	0·025	16·35	4·7
				24 hr. before testing
Experiment *B*: Liver fraction I 0·2 mgm./mouse				
Treated	5	0·030	14·1	4·3
Controls	5	0·020	14·8	4·0
Experiment *C*: Liver fraction I 0·4 mgm./mouse				24 hr. before testing
Treated	5	0·027	14·1	4·2
Controls	5	0·020	14·8	4·0
Experiment *D*: Liver fraction I 0·4 mgm./mouse				48 hr. before testing
Treated	5	0·021	13·7	3·7
Controls	3	0·027	15·3	4·5
Experiment *E*: Liver fraction II 0·4 mgm./mouse				24 hr. before testing
Treated	5	0·022	13·0	4·5
Controls	3	0·026	13·7	4·0

All animals tested with 16 mgm. carbon/100 gm. mice intravenously.
All liver fractions were given intraperitoneally.
* Ratio, body-weight to weight of liver and spleen.

Table 2. Effect of Liver Fractions (L.F.) on the Experimental Infection by *Salmonella Dangsz* in Mice

Infection*	Substance	Dose intraperitoneal route	Time of challenge (hr.)	Mean survival time (days)
1,000 germs of *Salmonella Dangsz* (intravenously)	Control	—	6	4·4
	L.F. I	0·20 ml./20 gm.	6	5·0
700,000 germs of *Salmonella Dangsz* (intraperitoneally)	Control	—	6	3·55
	L.F. I	0·20 ml./20 gm.	6	4·1
	L.F. I	2 × 0·20 ml./20 gm.	first injection, after 6 hr.; second injection, after 48 hr.	4·1

* 10 mice/group.

The liver fractions used are designated fractions I and II and were administered in doses of 0·2 mgm. dry substance per animal. The substance was dissolved in twice-distilled, pyrogen-free water and injected intraperitoneally. The control mice received saline injections. The phagocytic function of the reticulo-endothelial system was measured by the kinetics of blood clearance of 16 mgm./100 gm. mice of colloidal carbon (C11/1431*a*) according to the method described previously (ref. 3 and unpublished work by Dedichen, J., Laland, P., and Laland S.). The test was carried out 6, 24 and 48 hr. after the administration of the liver fraction. The results are shown in Tables 1 and 2. Stimulation of phagocytic activity could not be established by the method used.

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Abnormalities in the Fine Structure of the Neuromuscular Junction in Patients with Myasthenia Gravis

In a recent communication, Bickerstaff *et al.*[1] were unable to demonstrate differences between the synaptic regions of myasthenic and non-myasthenic patients when muscle biopsies were examined by electron microscopy.

Although a detailed study of the fine structure changes in several biopsied cases of myasthenia gravis is being prepared for future publication, we would like to report at this time that definite alterations in both the presynaptic and postsynaptic regions of the neuromuscular junctions do occur in patients with myasthenia gravis.

Muscle biopsies were obtained from intercostal muscles and peripheral muscles of myasthenic patients without recourse to methylene blue staining or electrical stimulation and recording. Normal human endplates for examination were obtained from children and adults subjected to thoracotomy for repair of congenital or acquired cardiac defects.

Pieces of muscle obtained at the time of primary muscle incision were placed in buffered (*p*H 7·35) 4 per cent formol-sucrose fixative[2] for 15–20 min., washed and then put buffered (*p*H 7·35) into 1 per cent osmium tetroxide for 15 min. The blocks of muscle were rapidly dehydrated in graded ethanol and embedded in mixtures of 30 per cent methyl methacrylate and 70 per cent butyl methacrylate or 'Epon 812' (Shell Chemicals, New York). Thick sections were examined by phase microscopy and the blocks were trimmed to contain selected endplate areas. Silver sections were studied in an RCA *EMU 3D* electron microscope.

Two kinds of abnormalities were observed in the myasthenic neuromuscular junctions: (*a*) focal areas of decreased electron density in the normally electron-dense portion of the sarcolemmal membrane within the secondary synaptic clefts; (*b*) extensive disorganization of endplate structure characterized by shrunken axon filaments, decreased numbers of secondary synaptic clefts, widening and clubbing of secondary synaptic clefts, and decreased numbers of mitochondria in the sole plate area.

Figs. 1 and 2 illustrate the appearance of a normal human neuromuscular junction. The axon terminal filament (*A*) and overlying Schwann cell (*S*) are separated by the primary synaptic cleft (*PSC*) from the elaborately infolded sarcolemma which forms the secondary synaptic clefts (*SSC*). A mitochondrion in the axon filament is present at *M*. Fig. 2 shows a drawing illustrating the relationships of these structures and the finely granular 'basement membrane' (*BM*) within the synaptic clefts. Figs. 3 and 4 illustrate disorganization of the secondary synaptic clefts and the moth-eaten appearance of the sarcolemma in the secondary synaptic clefts of a myasthenic neuromuscular junction. Figs. 5 and 6 illustrate at greater magnification the clubbing of the secondary synaptic clefts and the focal loss of material in the sarcolemma within the clefts.

In many of the endplates examined, abnormalities in the layered 'basement membrane' within the synaptic clefts were observed. Fig. 3 shows a single layer of 'basement membrane' in most areas whereas Fig. 5 shows loss of layered 'basement membrane' in most areas.

Pore-like defects in the axolemma described by Bickerstaff *et al.*[1] were seen in normal neuromuscular junctions as reported by others[3].

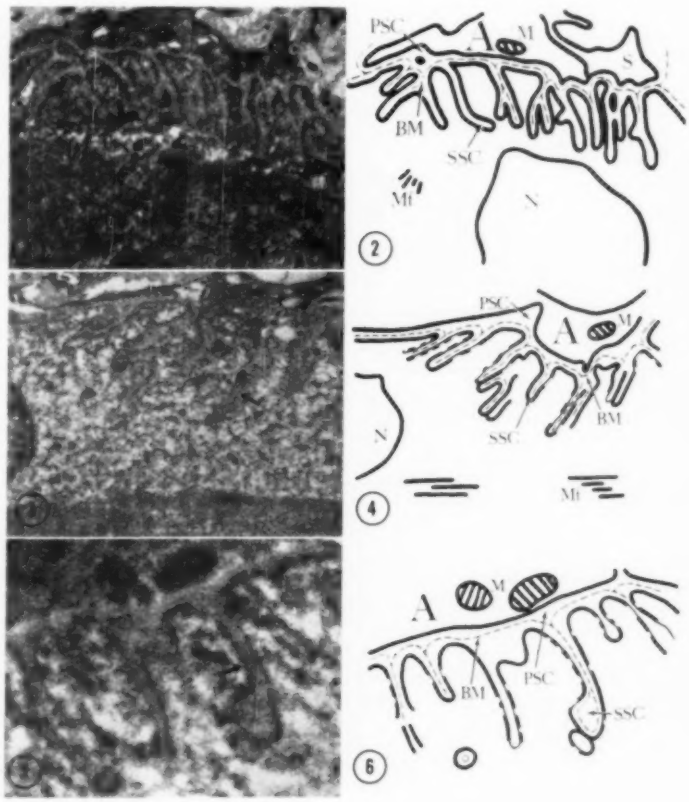

Fig. 1. Electron micrograph of neuromuscular junction from a non-myasthenic patient. The three major components of the synapse, Schwann cell, axon filament and post-synaptic apparatus, are illustrated. Note the layered 'basement membrane' within the secondary synaptic clefts. (× *c.* 16,300.) Fig. 2. Diagram of non-myasthenic neuromuscular junction showing major structural components and 'basement membrane' (dashed lines) within the synaptic clefts. Fig. 3. Electron micrograph of myasthenic neuromuscular junction showing disorganization of the synaptic clefts and focal areas of thinning and disruption of the sarcolemma within the secondary synaptic clefts (marked with arrow). (× *c.* 16,000). Fig. 4. Diagram of myasthenic neuromuscular junction prepared from Fig. 3 showing the changes illustrated in Fig. 3. Fig. 5. Electron micrograph of myasthenic neuromuscular junction showing swelling and clubbing of secondary synaptic clefts, moth-eaten appearance of the sarcolemma within the secondary clefts and loss of layering of the 'basement membrane' within the secondary clefts. (× *c.* 24,000.) Fig. 6. Diagram of myasthenic neuromuscular junction prepared from Fig. 5 showing the changes illustrated in Fig. 5

A, Axon filament; *BM*, 'basement membrane'; *M*, mitochondria; *Mf*, muscle filaments; *N*, nucleus; *PSC*, primary synaptic cleft; *S*, Schwann cell; *SSC*, secondary synaptic cleft

Although it is premature to attempt to correlate the abnormalities observed in the fine structure of myasthenic neuromuscular junctions with the physiological abnormality in these patients, our investigations indicate that definite morphological alterations occur which may be related to the functional disability.

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BIOLOGY

Variation in the Secondary Sex-Ratio of the Grey Seal *Halichoerus grypus* (Fab.) during the Breeding Season

Hewer[1] has suggested that the secondary sex-ratio (that is, the sex-ratio at birth) of the grey seal is probably close to equality. Since this publication, considerably more data have been collected on the grey seal colony on the Farne Islands, Northumberland, by members of the Natural History Society of Northumberland, Durham and Newcastle upon Tyne. Of 1,433 calves which were tagged, sexed and aged between 1952 and 1959 inclusive, 731 were males and the remaining 702 females; a result which does not differ significantly from a 1 : 1 sex-ratio and which confirms Hewer's findings.

Despite the very nearly equal sex-ratio obtained, distinct differences were found when the sex-ratio was examined in relation to the time of the breeding season. Coulson and Hickling[2] have shown that there is little annual variation in the breeding season of the Farne Island colony of grey seals, and it is therefore reasonable to group data collected over a number of years into the same fortnightly periods. As is shown in Table 1, there is a distinct tendency for the sex-ratio to change from a preponderance of males at the beginning of the breeding season (in late October) to a markedly higher proportion of females at the end of the breeding season ($\chi^2 = 8{\cdot}56$, 3 d.f., $P < 0{\cdot}05 > 0{\cdot}01$). This result could be produced by the male calves being born, on average, earlier than the female calves. This, in fact, does occur but the difference is small, the average difference being less than 3 days.

Table 1. Sex-Ratio of Grey Seal Calves on the Farne Islands according to their Date of Birth

Year	Date of birth							
	Oct. 14–27		Oct. 28–Nov. 10		Nov. 11–24		After Nov. 24	
	♂	♀	♂	♀	♂	♀	♂	♀
1952	8	4	16	18	12	8	8	8
1953	12	8	11	16	5	10	3	8
1955	5	8	43	42	20	25	9	14
1956	7	6	43	47	47	47	24	32
1957	36	22	114	96	67	60	13	18
1958	1	1	57	38	45	38	11	10
1959	2	2	69	61	34	41	9	14
Total	71	51	353	318	230	229	77	104
Sex-ratio	100 : 71·8		100 : 90·1		100 : 99·6		100 : 135·1	

While seasonal differences in the sex-ratio of domestic and laboratory mammals have been recorded by Parkes[3], this type of difference in the sex-ratio has not been recorded before in the Phocidae.

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Dissociation of Isohæmagglutinin Formation and Tolerance of Skin Grafts in Chicks

The administration of homologous whole blood into the embryo or new-born animal can produce either tolerance of skin grafts[1] or lead to the suppression of the isohæmagglutinin formation[2]. The causal relationship between these two types of immunological areactivity, however, remains obscure. It could be due to the fact that an identical antigenic stimulus is needed for agglutinin formation and transplantation immunity. There is evidence that red blood cells and some other tissue cells have some antigens in common. After the transplantation of tumours in mice and rats[3] and after the transplantation of skin in mice, rabbits and chicks[4], agglutinin formation was revealed even in those instances where the participation of red blood cells transferred in the graft could be ruled out. On the other hand, at least in mammals, red blood cells alone were not able to produce immunity against skin grafts[5].

In the present experiment, we investigated the formation of isohæmagglutinins in 13 chicks tolerating skin grafts after previous immunization with blood of the donor of the graft. Tolerance was produced in six individuals by mutual application of the skin graft immediately after hatching, in seven individuals by a similar skin transplantation with simultaneous administration of 0·5 ml. of heparinized blood of the donor. At the age of 6–12 weeks the tolerant chicks with the feathered graft, which had taken, were immunized with six 1-ml. doses of fresh citrated blood of the donor, administered intravenously. Plasma specimens for estimating the agglutinin titres were withdrawn in three-day intervals for two weeks after immunization was started.

In 10 from a total of 13 chicks tolerating the skin graft on the sixth to tenth day after the beginning of immunization, the formation of isohæmagglutinins against red blood cells of the donor of the graft and blood was detected (Table 1). The antibody response was relatively uniform, the maximum titres being 1/8–1/16. The grafts remained even after immunization in most chicks tolerating the graft for at least six weeks without any signs of destruction. Only in two animals they disintegrated between the fourth and sixth week after immunization. The immune response following the immunization by blood of the donor thus did not influence the fate of the tolerated homografts. Agglutinins developed in all animals where the tolerance was produced by the graft alone.

Table 1

Tolerance induced on the first day after hatching by	No. of animals	Maximal titres of agglutinins after immunization	No. of animals with feathered grafts more than 6 weeks after immunization
Skin grafting	6	16, 16, 16, 16, 8, 8	4
Skin grafting and whole blood	7	16, 16, 8, 8, 0, 0, 0	7

Two grafts were destroyed between the fourth and sixth weeks after immunization. Three tolerant animals did not produce agglutinins even after repeated immunization.

but only in 4 out of 7 chicks where the tolerance was produced not only by the graft but also by the administration of blood on the first day after hatching. The remaining three tolerant animals did not develop any agglutinins, even after repeated immunization. Serological evidence was provided that the erythrocytes of the donors differed as to their antigens from those of their tolerant partners. These three animals not only tolerated grafts but also the red blood cells which were administered to them immediately after hatching.

From the results it appears that the cells of the skin graft alone are not capable of producing tolerance for red blood cell antigens. This is the reciprocal picture of the former finding that erythrocytes alone, administered during the adaptive period, are unable to produce tolerance of the skin graft in chicks[6]. If we can assume that this dissociation is caused by the antigen difference of red blood cells and tissue cells, then it can be also concluded from our results that some erythrocyte antigens are absent in tissue cells.

It cannot be ruled out, however, that the dissociation of both types of tolerance could be caused by factors other than antigen differences between erythrocytes and the cells of the skin graft. It is, for example, possible that the transplantation alone on the first day after hatching produces in the chicks some type of a local immunological tolerance. Finally, the temporarily tolerated skin graft could survive further also on grounds other than the persistence of the state of specific immunological activity of the recipient.

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Inhibition of the Development of a Marine Sessile Community

Between October 1958 and September 1959 two panels of 'Tuffnol', each 2 ft. square, were suspended on either side of a raft at Port Royal, Jamaica. The purpose of these panels was to collect data on the settlement of an ascidian, *Ascidia nigra*. Each panel was examined at 2-monthly intervals, the two panels being examined on alternate months. When a panel had been examined it was cleaned before replacement on the raft. In this way a fresh settlement surface was provided each month. In the course of the two months in which a panel was exposed a dense growth of sessile animals always developed on it, usually dominated by *Balanus amphitrite* and *Didemnum maculosum*, with smaller numbers of other ascidians (*A. nigra*, *Diplosoma macdonaldi*, *Symplegma viride*, *Polyclinum constellatum*), serpulid worms, lamellibranchs, bryozoans and the alga *Enteromorpha sp.*

On October 1, 1959, it was necessary to find an alternative place to hang the panels, and they were moved to another raft close which already had hanging from it six panels that had been in the water continuously for 26 months. These latter panels were dominated by a community of sponges of several species, sea anemones (*Aiptasia tagetes*) and ophiurans (*Ophiothrix angulata*) with an associated fauna of crustaceans, polychaete worms, and molluscs. There were very few ascidians in these communities.

The panel which was raised and examined on November 1, 1959, had a fairly normal community on it; but it should be noted that this would have developed from larvæ settling before the panels were shifted. The panel examined on December 1 had been in the new position for the whole of the 2 months of exposure, and had a completely different appearance from anything hitherto seen. Considerable portions of the panel had not been colonized at all, and elsewhere there were only small numbers of barnacles and serpulids, a few sponge colonies, a few colonies of the ascidian *Botryllus planus* and 16 specimens of *A. nigra*. On January 4, when the other panel was again examined after 2-months exposure at the new site, the effect was more marked. Barnacles and serpulids were almost entirely absent from this panel, there were no *A. nigra*, only one small colony of *D. maculosum*, and along one margin of the panel there were several oysters (*Isognomon alatus*). Otherwise small thin sponge colonies and a few filaments of algæ were the only noticeable colonisers.

The reduction in colonization was not due to a reduction in available larvæ or to any physical change in the environment such as temperature or salinity changes in the water. This is amply demonstrated by the fact that on a similar raft, moored 20 ft. from this one, normal colonization occurred. This other raft had eight clean panels attached to it on October 1, and by December 1 they were all covered by a *Balanus-Didemnum* community with all the usual associated animals. Only four of these panels were on the same level in the water as the test panels on the other raft; these had an average of 28 *A. nigra* on each.

Four of the above eight panels were removed on December 1 and replaced by clean panels. By January 4 the latter had developed a normal *Balanus-Didemnum* community, and the two panels on the level of the test panels had 48 and 51 *A. nigra* respectively. Observations could not be continued into 1960.

It is clear from the foregoing observations that development of a normal sessile community was inhibited on the two panels inserted in among the mature sponge-anemone-ophiuran community, and it is also clear that this was a purely local effect not observed 20 ft. away. In every respect other than a small difference in panel size and the presence of the sponge community the two environments seemed

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identical. Each raft was the same size and in the same depth of water and the arrangement of the panels on them was the same in each case. The inhibition was not due to any ageing effect of the panels as the same panels developed normal communities at a later stage when removed from the sponge community. The only possible explanation is that the mature sponge-anemone-ophiuran community actively inhibited the development of a primary community on the clean panels. It is not possible at present to say what form this inhibition takes: it could either prevent larval settlement or prevent survival and growth of young sessile stages. The absence of large barnacle settlements suggests the former possibility as dead shells would probably persist if metamorphosis had occurred. Nor is it possible to say what is its cause, but it is probably an attribute of the sponges rather than other members of the mature community. The high filtration-rate of a sponge community could deplete the surrounding water of food for the young primary colonizers, or the secretion of mucus or chemical toxin might kill the young stages.

Acknowledgement is made to the Nuffield Foundation for receipt of a research grant at the time these observations were made.

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The Deepest Recorded Fishes

THE number of fishes from the hadal zone (in depths between about 6,000 and 11,000 m. in the deep-sea trenches) is very limited. The *Princesse-Alice* collected *Bassogigas profundissimus* (Roule) at 6,035 m. in the east Atlantic Ocean[1], the *Galathea* collected a species of Liparidae (Kermadec Trench, 6,660–6,770 m.) and *Bassogigas* sp. (the Sunda Trench, 7,160 m.)[2], and the *Vitjaz* collected *Careproctus* (*Pseudoliparis*) *amblystomopsis* Andriashev and another species of that genus from the Kurile-Kamtchatka Trench (7,210–7,230 m.) and from the Japan Trench (6,156 and 7,587 m.)[3–5]. Thus, the last-named depth is the hitherto greatest known depth from which any fish has been brought up.

During the truly remarkable dive of the U.S. Navy bathyscaphe, the *Trieste*, in the Mariana Trench in January 1960, the vessel remained on the bottom for 20 min. at a (corrected) depth of 35,800 ft. (10,912 m.) The only living creatures observed by the two men on board, Engineer Jacques Piccard and Lieut. Don Walsh, were a "shrimp" and an animal which Piccard[6] described as "a true fish", being "apparently of the sole family, about a foot long and half as wide. . . . [It] moved away from us, swimming half in the bottom ooze, and disappeared . . ." (p. 235). It was "tentatively described as *Chascanopsetta lugubris*" (p. 230). Walsh[7] mentioned it as a "flat-fish" which was "white and about a foot long".

There are several reasons for considering these statements as being somewhat dubious. First, flatfishes are commonly known as a primarily littoral order with a number of bathyal, but no single truly abyssal species (Chabanaud's record[8] of *Bathysolea profundicola* (Vaillant) having been captured between 2,000 and 4,000 m. depth is erroneous, the species being known only from between 250 and 1,290 m.). The only two species which penetrate beyond 1,500 m. are *Citharichthys dinoceros* Goode and Bean (201–1,746 m.) and *Poecilopsetta beani* (Goode) (203–1,639 m.), both from the West Indies. The deepest recorded flatfish from the *Galathea* Expedition was from 750 m. depth[9], and no flatfish was collected in or close to any of the trenches investigated. *Chascanopsetta lugubris* Alcock was previously recorded only between depths of 220 and 977 m.

Secondly, it seems very probable that certain groups of the trench fauna have a distinct lower limit. Decapod crustaceans and bryozoans are certainly not able to penetrate into the hadal zone and other important marine groups such as cirripeds, asterids, echinids, tunicates, and fishes have not been recorded at depths exceeding some 7,000–7,500 m.[10]. It is true that the number of trawlings deeper than 7,500 m. is limited to (at least) 22, but the majority of these catches have constantly yielded representatives of the really significant, hadal animals, such as actinians, polychaetes, isopods, amphipods, prosobranchs, lamellibranchs, and holothurians. Negative records are naturally of less value, but should be taken into account also.

Thirdly, it seems to appear from most of the observations made from bathyscaphes that even zoologists have great difficulties in recognizing the creatures seen through the porthole. In the case in point the animal was observed "swimming half in the bottom ooze". If it was not a fish, its remarkable size would indicate that it was probably some kind of holothurian, for example perhaps related to the bathypelagic, cushion-shaped *Galatheathuria aspera* (Theel). Hansen and Madsen[11] found the gut of this extraordinary animal to be partly filled with remains of pelagic forms and with various bottom foraminiferans and sponge spicules. The animal is almost 1 ft. long and oval in outline.

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A New Intermediate Host of Schistosome Trematodes from New South Wales

RECENTLY schistosome larvæ have been discovered in the snail *Siphonaria denticulata* Quoy and Gaimard. Cercariæ from infected snails cause a typical schistosome dermatitis in man.

Schistosome dermatitis occurs along parts of the coast of New South Wales. Infections usually occur in sandy estuarine lakes where the snail *Velacumantus australis* (= *Pyrazus australis*) harbours the schistosome, *Austrobilharzia terrigalensis* Johnston[1]. However, cases of schistosome dermatitis have occasionally been reported from marine rock pools where no *Velacumantus* snails occur. An examination of a number of different species of snails from such places showed that *Siphonaria denticulata* harboured schisto-

some cercariæ. A typical schistosome dermatitis followed exposure to these cercariæ.

An examination of 100 *Siphonaria* from part of a rock platform at Cape Banks, Sydney, showed an infection-rate of 35 per cent. At low tide this area is often crowded with the gull *Larus novæ-hollandiæ*.

Twenty-five budgerigars (*Melopsittacus undulatus*) were exposed to naturally emerged cercariæ, or cercariæ from crushed snails. Immature schistosome worms were recovered from the liver or lungs of five birds. The worms appear to belong to the sub-family Bilharziellinae.

It is interesting to note that the host snail, *Siphonaria*, belongs to a pulmonate family (the Siphonariidae). Members of this family bear a superficial resemblance to limpets, but may be distinguished from them by a groove which runs down inside the right-hand side of the shell. Members of the Siphonariidae are normally found in the upper littoral zone of rocky shores. Their distribution is almost world wide, but they are especially common around the shores of the Pacific and Indian Oceans[2].

Because the Siphonariidae have such a wide geographical distribution, and their normal habitat is often the resting place of birds of the seashore, one might expect them to be the hosts of larval schistosomes in many other places.

The assistance of Mr. A. J. Bearup is gratefully acknowledged.

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Transmission of Gall-Diseases of Cacao, Mango, and Pigeon Pea

'Cushion-gall' disease of cacao is widely distributed throughout South America[1] and has been reported also from Ghana[2] and Nigeria and Ceylon[3]. The disease has been found in most old cacao plantings in British Guiana, in the 'green-point' form, and was recorded and described by A. W. Bartlett[4] as long ago as 1905, although his report was only rediscovered in 1959. The presence of the 'flowery' type has yet to be confirmed.

Hutchins[5] has transmitted the disease successfully in Costa Rica by tissue implantation, while workers in Ghana (Tinsley, T. W., personal communication, November 1959) have transmitted a similar disease using the single cotyledon technique.

In the present work the 'green-point' type gall of cacao was transmitted by using the half-bean technique: galls were produced three weeks to a month after inoculation. Washings from the surface of galls, or extracts of macerated gall tissue transmitted at a rate of 1/7. The germination-rate of half-beans treated with gall inoculum was markedly lower than that of controls treated with distilled water.

Galls similar to the 'green-point' form of cacao have been found on mango and pigeon pea. Distilled water washings, and extracts of gall tissue of these species were inoculated into cacao half-beans. Galls were visible in the axils of the cotyledons about one month after inoculation.

The transmission-rates were:

	Washings		Tissue extract	
Mango	13/35	16/25	15/35	17/25
Pigeon pea	7/25		9/25	

The galls produced by inoculation from mango material were indistinguishable from those produced by inoculations from cacao 'green-point' material. While most of the galls produced on plants inoculated with pigeon pea gall were similar to cacao-gall, in some, the axillary bud enlarged very considerably and became chlorotic, with no proliferation of other buds. The germination-rate of the treated plants was comparable with those of controls with distilled water.

Transmission of the mango gall into a two-month cacao seedling was also obtained by inoculation of the axillary bud with tissue extract.

In the absence of any knowledge of vectors of 'cushion-gall' of cacao the significance of these results is difficult to assess. However, the ease with which the diseases of mango and pigeon pea can be transmitted to cacao under laboratory conditions would suggest that the cultivation of these two species in close proximity to cacao should be avoided.

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J. F. Archibald

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Puccinia polysora on *Tripsacum laxum* and *Zea mays*

There would appear to be the impression that, in the Carribbean, the same strain of *Puccinia polysora* attacks both *Tripsacum laxum* (Guatemala grass) and *Zea mays*. In Trinidad during 1953–54 an attempt to cross-inoculate uredospores from the two species proved completely unsuccessful. Successful inoculation of the same species was a matter of routine. It was not possible to detect any morphological differences between the strains, but they are certainly quite distinct. *T. laxum* is at present free from attack by *P. polysora* in Eastern Nigeria.

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MICROBIOLOGY

Slime-wall Formation in the *Salmonellae*

The formation of a 'slime wall', which is usually a property of *Salmonella paratyphi B* but not of *S. paratyphi B* var. *java*, has long been used as a criterion of differentiation between these two organisms[1–4]. According to Birch-Hirschfeld[3], the slime-wall consists of a nitrogen-free polysaccharide containing more than 40 per cent of glucose. It is formed on solid media, optimally at temperatures of about 20–25° C. and not at 37° C. In this laboratory it is regularly demonstrated by incubating platings on solid media, initially at 37° C. overnight, and afterwards at 21° C. The slime-wall is usually evident after 24 hr. at 21° C. In the search for a reliable medium on which to demonstrate its formation, it was found that the

concentration of phosphate exerted a powerful influence on the production of the polysaccharide. The basic solid medium used in these experiments contained 2 per cent of 'Bacto' dehydrated nutrient broth (Difco Laboratories), 0·85 per cent sodium chloride and 1·2 per cent New Zealand powdered agar ; it is referred to hereafter as Difco agar. Sörensen buffer, *p*H 7·0, was mainly used as the phosphate source. It was added to Difco agar in concentrations of *M*/5 doubling in dilution to *M*/160 ('phosphate agar'). The favourable effect on slime-wall production was strongest at *M*/5 and diminished progressively with the fall in phosphate concentration, little effect being observed beyond *M*/20, which was adopted as the lowest phosphate concentration for routine use. In strains of *S. paratyphi B* that were slime-wall positive on Difco agar, the amount of slime produced was greatly increased in the presence of phosphate. Strains that formed slime in small amounts or irregularly on nutrient agar produced it in abundance when phosphate was added. Some cultures that were consistently negative on nutrient agar secreted slime on *M*/5, *M*/10 and *M*/20 phosphate agar, others on *M*/5 and *M*/10, and yet others on *M*/5 phosphate agar only.

I was able to classify *S. paratyphi B* by these reactions. Strains that produced slime freely on Difco agar corresponded to classical *S. paratyphi B* and did not ferment D-tartrate. Strains forming slime sparsely or not at all on Difco agar, but abundantly on the same medium reinforced with *M*/20 Sörensen buffer, were mostly isolated from cases of food poisoning, but occasionally from cases of enteric fever. These were usually D-tartrate positive. Strains that formed slime only on *M*/5 phosphate agar were D-tartrate positive and came almost entirely from cases of food poisoning, although one strain reacting in this way has caused enteric fever. The typing phages of Felix and Callow[6,7] divided these strains into groups of types characteristic of each of the three varieties described. Exceptions to these reactions, in addition to the one already quoted, were found, however ; for example, one phage type, associated only with food poisoning, was slime-wall negative and D-tartrate negative. From this stock I have isolated both slime-wall positive and D-tartrate positive clones. It has been possible in a number of other strains to isolate slime-wall negative mutants from slime-wall positive stocks, and vice versa (see ref. 2). Within slime-wall positive lines, mutants were found that varied in the amount of slime they produced. These variations were often apparent only on phosphate agar.

An exploration of organisms of every group of the Kauffmann White scheme of *Salmonella* serotypes revealed that, while very few indeed synthesized slime on Difco agar, the great majority produced it on phosphate agar. The most abundant production of the polysaccharide was on media containing *M*/5 phosphate, and some strains produced it only on such media. Others were able to form it when the phosphate concentration was reduced to *M*/10, and yet others on *M*/20 phosphate agar. The slime wall is uniform in appearance throughout all the *Salmonellae* tested, usually taking the form of a raised marginal ring, clearly demarcated and opaque by transmitted light and rather 'silky' when viewed by oblique illumination. Obvious slime production occurs only when the *p*H is 6·5 or higher. Between *p*H 7·0 and *p*H 8·0 it is formed freely, *p*H 7·0 being used as a routine in my experiments. Below *p*H 6·5 the colonial morphology is 'rough'.

Buffers other than Sörensen's were tried at *p*H 7·0 ; but few stimulated better slime formation than unbuffered Difco agar. Sodium glycerophosphate was very active, however, and a concentration of *M*/5, adjusted to *p*H 7·0 with sodium dihydrogen phosphate or hydrochloric acid, produced colonies that were completely mucoid after 24 hr. at 21° C. The metallic ions in the phosphates were not essential for slime-wall synthesis, for glycerophosphoric acid adjusted to *p*H 7·0 with ammonium hydroxide was equally active.

The presence of a fermentable carbohydrate, in the form of 0·5 per cent glucose, increased the amount of slime formed but was not essential for its synthesis in strains that produced it freely on Difco agar. Some strains forming slime only on phosphate agar, however, required the addition of glucose for its production. (The basic Difco medium employed in these experiments contained no detectable reducing sugar.)

The slime is not formed under anaerobic conditions.

It is not yet apparent whether the phosphate operates purely as a non-toxic buffer that does not inhibit slime-wall synthesis, or whether it participates in the synthesis. Some of the other buffers tested were clearly inhibitory in the higher concentrations used.

Whether or not the polysaccharide of which the slime is formed is identical in all *Salmonellae*, it is evident that the system that synthesizes it is similar throughout. This system is now under closer examination. Work is in progress on the conditions governing slime formation, the chemical and immunological nature of the polysaccharides, and on the possible effects of phosphate on the elaboration of other antigens. The results of these investigations will be published at a later date.

Note added in proof. An exploration of other members of the Enterobacteriaceae, for example, *Escherichia coli* and *Arizona*, has shown that the phenomenon of slime-wall formation in the presence of relatively high phosphate concentrations is widely distributed in this family.

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CYTOLOGY

Chromosomes of the Wild Mushroom

Very little work has been done on the cytology of the wild mushroom *Agaricus campestris* Fr. var. *tetrasporus*. Most investigations have been confined to cultivated mushrooms (reviewed by Evans[1,2]). The cytology of the wild form is also of considerable interest since such information may contribute to our understanding of why it has not been possible to

cross the wild with the cultivated form in attempts at introducing commercially desirable characters, such as an improved flavour.

Colson[3] examined both varieties of mushroom and found that the haploid chromosome number, seen as bivalents at meiosis, was 9 in both varieties. In a variety grown on a commercial scale in Great Britain, Evans[1] found a higher haploid chromosome number, $n = 12$, which he attributed to either: (*a*) different strains of the fungus having different chromosome numbers or (*b*) differences in chromosome number being due to limitations of technique. Previous observations were made on sectioned material whereas Evans's observations were made by means of a squash technique which facilitated study of entire cells.

Since the only previously recorded chromosome number of the wild mushroom was by means of a section technique, the work reported here was carried out by means of a squash technique in order to ensure that entire cells were being examined.

Fruit-bodies of the wild mushroom were collected from permanent pasture land at Aberystwyth, at the stage when the veil had just ruptured revealing part of the hymenium. Gills, at this stage, were fixed in Evans's mixture[1] of chloroform, ethanol and glacial acetic acid (7 : 5 : 2) immediately, in the field. Squash preparations were obtained with acetic orcein after sufficient hydrolysis of tissue with hydrochloric acid (to remove basophilly of the cytoplasm) for the study of meiosis in the basidium. Twelve bivalents were observed at the first division of meiosis. The clearest count obtained was at diakinesis (Fig. 1). It was more difficult to separate the bivalents after they had become orientated around the metaphase plate. Another difficulty in counting bivalents was non-synchronization of separation of chromosomes of the bivalents, at late metaphase–early anaphase.

Thus the chromosome number of both wild and cultivated mushroom varieties, as determined by a squash technique, is $n = 12$, which supports the suggestion of Evans[1] that "previous counts may have erred on the low side" due to the inadequacy of the sectioning method for chromosome counting.

It appears that the failure to hybridize the wild and cultivated varieties[4] does not simply depend on a difference in chromosome number. It is possible that an incompatibility system[5] and a difference in breeding system mechanism are involved. Thus research on the breeding mechanism, so far, indicates that the cultivated (2-spored) variety is a homothallic heterokaryon[3,6], whereas the wild variety is a heterothallic heterokaryon like most other 4-spored hymenomycetes[4].

This work was conducted at the Department of Agricultural Botany, University College of Wales, Aberystwyth, under the direction of Prof. P. T. Thomas, whose help and encouragement are gratefully acknowledged.

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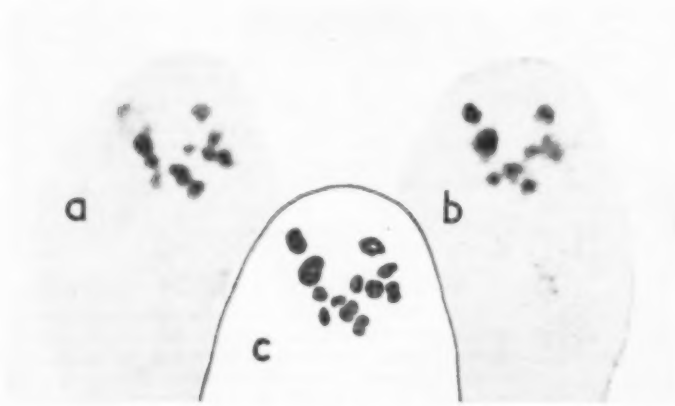

Fig. 1. Twelve bivalents at diakinesis. *a* and *b*, Photomicrographs at two foci; *c*, drawing of the group of bivalents as seen under the microscope. (× 6,000)

GENETICS

Glutamic Dehydrogenase in Single-Gene Mutants of *Neurospora* Deficient in Amination

Fincham[1,2] described some amination-deficient (*am*⁻) mutants of *Neurospora crassa* which lacked the glutamic dehydrogenase and, therefore, could grow only very slowly in minimal medium in the absence of exogenous L-glutamic acid. Normal growth of the *am*⁻ mutants occurred in media containing glutamate, aspartate, alanine, ornithine or arginine, but not glycine, serine, threonine, histidine, lysine or citrulline[2]. The effectiveness of various amino-acids in supporting the growth of the *am*⁻ mutants was later correlated[3] to the efficiency of enzymatic transamination between these amino-acids and α-ketoglutarate in cell-free extracts. The growth of *am*⁻ mutants on exogenous sources of amino-acids is thus without doubt due to their conversion first to glutamic acid by transamination.

The very slow growth of the *am*⁻ mutants on minimal medium, however, has never been explained. It could perhaps be due to the formation of traces of glutamic acid by transamination between α-ketoglutarate and some other amino-acids initially synthesized by the cells. So far as we are aware, however, the only major path of entry of ammonia in *Neurospora* is the reductive amination of α-ketoglutarate. It is therefore difficult to visualize how the *am*⁻ cells produce other amino-acids in the absence of glutamic dehydrogenase. Earlier, Sanwal[4] had demonstrated the presence of two different glutamic dehydrogenases, one specific for diphosphopyridine nucleotide (DPN) and another for triphosphopyridine nucleotide (TPN) in a related fungus, *Fusarium*. In following up this work with wild-type

strains of *Neurospora crassa*, Sanwal and Lata[3] succeeded in separating and purifying the TPN- and DPN-specific glutamic dehydrogenases. The glutamic dehydrogenase of *Neurospora* was reported to be specific for TPN[2] but later found[4] to be non-specific with regard to its coenzyme requirement.

The discovery of two different glutamic dehydrogenases[3] raised some interesting questions pertaining to the one-gene one-enzyme hypothesis. If single-gene *am*⁻ mutants had lost the ability to grow in the absence of some exogenous source of L-glutamate, did it mean that one gene mutation had affected two different glutamic dehydrogenases? To test this point we used two *am*⁻ mutants, 32213 *R1a* and 47305 *A* (both single-gene mutants) obtained through the courtesy of Dr. M. B. Mitchell of the California Institute of Technology, Pasadena. The wild-type strain, *R*⁺, was kindly supplied by Dr. P. K. Issac of the Department of Botany, University of Manitoba. The strains were grown in shake cultures from a conidial inoculum[5] in the minimal medium *N* of Vogel[7] supplemented with 0·1 per cent L-glutamate and the specific activity of the DPN-specific and TPN-specific glutamic dehydrogenases was determined[3] in cell-free extracts of 24-hr. and 48-hr. mycelial growth. Table 1 summarizes the results of this investigation.

Table 1. SPECIFIC ACTIVITY OF DPN- AND TPN-SPECIFIC GLUTAMIC DEHYDROGENASES OF WILD-TYPE STRAIN *R*⁺, *am*⁻ *32213 R1a* AND *47305 A* OF *Neurospora*

Strain	Hr. of growth	DPN-enzyme	TPN-enzyme
R⁺	24	90	320
	48	87	101
32213 R1a	24	32	none
	48	63	none
47305 A	24	61	none
	48	83	none

It will be seen from Table 1 that the wild-type strain produces both enzymes, but the *am*⁻ mutants produce only the DPN-specific glutamic dehydrogenase. It is clear, therefore, that the mutation of one gene has led to the loss of only one enzyme, the TPN-specific glutamic dehydrogenase. The slow growth of the *am*⁻ mutants on minimal medium is now understandable on the basis of the presence of the DPN-specific enzyme, but it is not easy to understand why the mutants cannot grow as well as the wild-type strain in the minimal medium. We have demonstrated[3] that the affinity of the TPN-specific enzyme for α-ketoglutarate is higher than the DPN-specific enzyme, but this fact alone is not sufficient to explain the slow growth of the mutants unless it is argued that the DPN-specific enzyme is primarily a degradative enzyme and the TPN-specific enzyme is biosynthetic[4,5]. We shall publish data elsewhere in support of this argument.

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* Post-Doctoral Fellow of the National Research Council of Canada (1960–61).

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SOIL SCIENCE

Interpretation of the Upper Plastic Limit of Clays

THE upper plastic limit, or liquid limit, of clays is regarded as that water content at which sufficient free water is present to allow clay particles to slip past one another under a certain applied force. It can also be interpreted as the distance between particles or between structural units of particles at which forces of interaction between the clay particles become sufficiently weak to allow easy movement of particles or units relative to each other. This interpretation allows an easier explanation of the influence on the liquid limit of such factors as exchangeable ion, salt concentration and *p*H of the clay paste. For this interpretation it is convenient to define an 'interaction volume' for a unit mass of clay particles as that volume within which individual particles or units of particles interfere with the movement of adjacent particles or units. The interaction volume will decrease as the applied force increases.

In addition to the influence of exchangeable ions on the liquid limit, for which published results have been summarized[1], it is necessary to know the influence of electrolyte concentration since this controls interparticle forces and particle arrangement in many clay pastes. Liquid limit values were measured according to a standard soil mechanics procedure of determining the number of blows required to close a groove in the clay paste samples using the Casagrande liquid limit device. Three or four water contents were used for which the number of blows fell between 15 and 40, and the water content at the 25-blow point (the liquid limit) was read from a plot of water content versus the logarithm of the number of blows. Water content was expressed on oven-dry weight of soil corrected for the weight of salt. Values for liquid limit are influenced by the procedure and by the drying and preparation history of the sample. These factors were kept constant, and only relative values of liquid limit are discussed.

The dominant interparticle force in pastes of montmorillonite with monovalent exchangeable cations is a repulsion arising from osmotic activity of the diffuse ion-layer around the particles[2]. Fig. 1 shows the measured liquid limit of sodium montmorillonite at different concentrations of sodium chloride. An increasing salt concentration, which results in a decrease in interparticle repulsion, decreases the liquid limit. The repulsion between particles can be considered to determine the interaction volume, keeping the particles in a fixed configuration with respect to each other and preventing free movement. As the repulsion is decreased, the particles become free to move at lower water contents or lower interparticle distances, and the liquid limit decreases.

When the repulsion is decreased by substituting a divalent exchangeable ion such as calcium, the liquid limit is also decreased. However, for calcium montmorillonite, increasing salt concentration does not decrease swelling by the predicted amount, and in Fig. 1 it did not decrease the liquid limit appreciably. Repulsion between individual particles resulting in large interparticle distances is not the dominant force. The clay paste consists of units of particles separated by 9 Å. within the unit. Larger separations occur between these units[3]. This struc-

ture or particle arrangement, which changes little with increasing salt concentration, determines the interaction volume or the water content at which interaction between units is low enough to allow easy movement.

In kaolinite pastes interparticle forces also control the liquid limit through their influence on particle arrangement. The dominant influence of particle arrangement is shown in Fig. 2 by the values with distilled water. The untreated clay has a *p*H of 4 and the particles are flocculated in an edge-to-face arrangement which results in a high interaction volume[4]. The neutral clays with a *p*H of 6·5 are still flocculated but the forces of attraction are lower. Fewer edge-to-face perpendicular contacts result in a lower interaction volume. In the dispersed sodium-saturated clay at *p*H 10 the interparticle force-resisting movement is the repulsion between particles which keeps them in more parallel arrangement. This is low for the kaolinite and the effective interaction volume is small. With increasing salt concentration the structure of all samples changes to face-to-face particle arrangement[4] with lower interaction volume than the edge-to-face but higher than the parallel arrangement. If the minimum in liquid limit for the dispersed clay at 0·01 *N* sodium chloride is real, it may result from decreased repulsion due to increasing salt concentration which initially decreases interaction volume more rapidly than the flocculated particle arrangement increases it.

For other clays the variation of liquid limit with electrolyte concentration may show a different pattern depending upon the interaction volume resulting from the interparticle forces. Limited measurements with a clay from the St. Lawrence Lowlands, which contains illite and chlorite, show the liquid limit passing through a shallow maximum at intermediate salt concentrations. This could result from the formation of a flocculated structure which becomes more compact as repulsion decreases due to further increases in salt concentration.

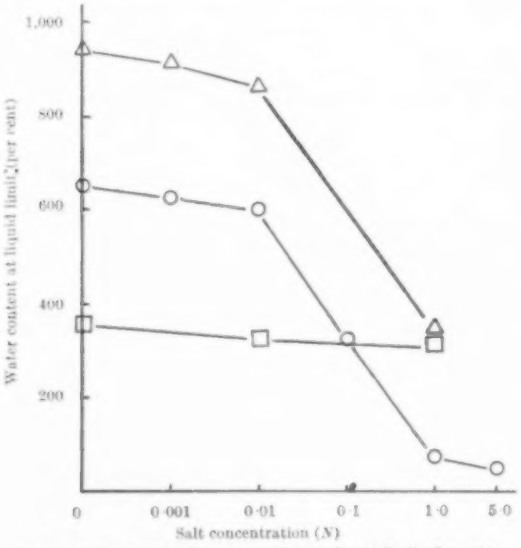

Fig. 1. Influence of salt concentration on liquid limit of montmorillonite clay with different exchangeable cations. △, sodium montmorillonite + sodium chloride; ○, natural bentonite + sodium chloride; □, calcium montmorillonite + calcium chloride

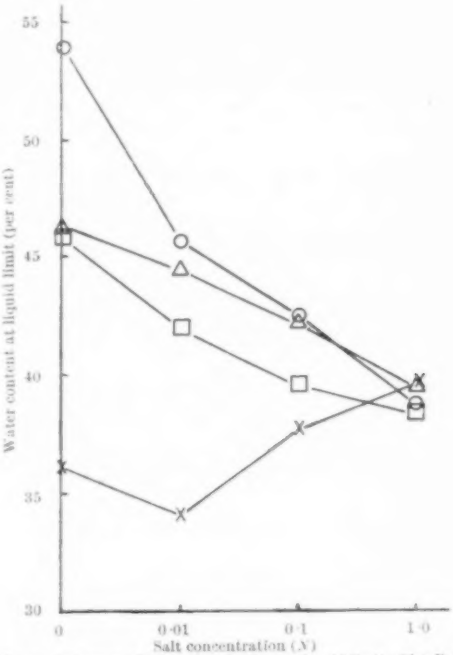

Fig. 2. Influence of salt concentration on liquid limit of kaolinite clay at different *p*H and with different exchangeable cations. ○, natural kaolinite (*p*H 4) + calcium chloride; △, sodium kaolinite (*p*H 6·5) + sodium chloride; □, calcium kaolinite (*p*H 6) + calcium chloride; ×, sodium kaolinite (*p*H 10) + sodium chloride

This interpretation of liquid limit controlled by interparticle forces explains why the liquid limit decreases with increasing valence of exchangeable ion for high-swelling clays, but increases for low-swelling clays where interaction volume is determined largely by particle arrangement. Here polyvalent ions lead to a more flocculated structure with a higher interaction volume.

At very high electrolyte concentration and in the presence of dissolving salt, clay pastes may become very stiff or show an increase in liquid limit. This effect has been termed ionotropy[5]. A definite structure or particle arrangement results from the salt diffusing into the clay paste. The intensification of *d* (001) spacings in X-ray diffraction patterns of salted clay pastes[6] indicates that the clay particles are in parallel orientation.

I wish to acknowledge the grant-in-aid of research from the National Research Council, Canada, under which this work was done, and the assistance of Mr. R. K. Chang, who made most of the measurements.

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Quebec.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, April 17

BRITISH SOCIETY FOR THE PHILOSOPHY OF SCIENCE (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. P. Alexander: "Science and Epistemological Atomism".

INSTITUTION OF ELECTRICAL ENGINEERS (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "The Education of Engineers—All's Well?" opened by Sir Hamish D. MacLaren, K.B.E.

SOCIETY OF CHEMICAL INDUSTRY, PESTICIDES GROUP (at 14 Belgrave Square, London, S.W.1), at 5.30 p.m.—Annual General Meeting.

INSTITUTE OF METAL FINISHING (at the Northampton College of Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Mr. J. Edwards: "Plating of Zinc-Based Die-Castings".

INSTITUTION OF MECHANICAL ENGINEERS, HYDRAULIC PLANT AND MACHINERY GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 7 p.m.—Discussion on "Co-ordinating the Needs of Hydraulic Machinery and Civil Engineering".

Monday, April 17—Tuesday, April 18

POWDER METALLURGY JOINT GROUP OF THE IRON AND STEEL INSTITUTE AND THE INSTITUTE OF METALS (at the Royal Commonwealth Society, Craven Street, London, W.C.2)—Discussion on "The Appraisal of Powders for Pressing and Sintering".

Tuesday, April 18

INSTITUTE OF FUEL (at the Royal United Service Institution, Whitehall, London, S.W.1), at 5.30 p.m.—Prof. Hoyt C. Hottel (Massachusetts Institute of Technology): "Radiative Transfer in Combustion Systems"* (Twenty-ninth Melchett Lecture).

Wednesday, April 19

BRITISH ASSOCIATION FOR COMMERCIAL AND INDUSTRIAL EDUCATION (at Senate House, University of London, W.C.1), at 10.40 a.m.—Conference on "New Routes to Further Education".

ROYAL METEOROLOGICAL SOCIETY (at 49 Cromwell Road, London, S.W.7), at 5 p.m.—Annual General Meeting and Presidential Address.

BONE AND TOOTH SOCIETY (at the Institute of Orthopædics, 234 Great Portland Street, London, W.1), at 5.15 p.m.—Dr. Franklin C. McLean (University of Chicago): "The Parathyroids and Vitamin D in Calcium Homeostasis".

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Dr. E. F. Drion: "The Intercorrelation between the Nutrients Consumed by a Group of Families in the Netherlands"; Mr. J. A. Heady: "Diets of Bank Clerks".

INSTITUTION OF ELECTRICAL ENGINEERS, SUPPLY SECTION (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. A. N. Arman, Dr. F. J. Miranda and Mr. G. R. Bishop: "Progress in Oil-Filled Cables and Their Accessories".

BRITISH INSTITUTION OF RADIO ENGINEERS, MEDICAL ELECTRONICS GROUP (at University College Medical School, University Street, Gower Street, London, W.C.1), at 6 p.m.—Dr. C. N. Smyth: "Instrumentation for Obstetrics".

INSTITUTION OF MECHANICAL ENGINEERS, EDUCATION AND TRAINING GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Undergraduate Project Work in Full-time and Sandwich Courses in Mechanical Engineering".

ROYAL SOCIETY OF ARTS (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Dr. K. L. Blaxter: "The Nutritional Physiology of Livestock Under Natural Conditions" (Fernhurst Lecture).

SOCIETY OF INSTRUMENT TECHNOLOGY, DATA PROCESSING SECTION (at 26 Portland Place, London, W.1), at 6.15 p.m.—Annual General Meeting, 7 p.m.—Mr. T. H. Flowers: "Electronic Telephone Exchanges".

Wednesday, April 19—Thursday, April 20

INSTITUTE OF RURAL LIFE AT HOME AND OVERSEAS (at the Colonial Office, Sanctuary Buildings, Great Smith Street, London, S.W.1), at 2.30 p.m. on Wednesday and 10.30 a.m. on Thursday—Eleventh Annual Conference on "The Land in Trust—at Home and Overseas".

Thursday, April 20

ROYAL SOCIETY (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. P. Benjamin and Mr. C. Weaver: "The Adhesion of Evaporated Metal Films on Glass"; Mr. C. J. S. Chapman, Mr. J. M. Gregory, Mr. R. W. Hill and Mr. M. W. Johns: "Nuclear Alinement of Cobalt and the Decay of Cobalt-55".

INSTITUTION OF MINING AND METALLURGY (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Annual General Meeting followed by Scientific Papers.

LINNEAN SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. R. Melville: "Bracken Regeneration from Sporelings"; Dr. John Ramsbottom: "A Letter from the Swedish Consul announcing the Arrival of the Linnean Collections"; Prof. L. J. Audus: "Recent Studies on Geotropism".

LONDON MATHEMATICAL SOCIETY (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. K. Stein: "On Holomorphic Maps in the Space of Several Complex Variables".

INSTITUTION OF ELECTRICAL ENGINEERS, UTILIZATION SECTION (joint meeting with the LONDON GRADUATE AND STUDENT SECTION, at Savoy Place, London, W.C.2), at 6 p.m.—Mr. P. J. H. Rata: "Aluminium in Electrical Engineering"; Mr. A. D. Swanston and Mr. B. W. Towell: "Diesel Railway Locomotives"; Mr. T. E. S. Rickard: "Automatic Programming for Hot Reversing Mills".

SOCIETY OF CHEMICAL INDUSTRY, ROAD AND BUILDING MATERIALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Annual General Meeting, followed by Mr. C. H. C. Brown: "Some Laboratory Investigations in connexion with the Development of Cationic Bitumen Emulsions".

Thursday, April 20—Friday, April 21

BRITISH KINEMATOGRAPH SOCIETY, and the TELEVISION SOCIETY (at the Institution of Electrical Engineers, Savoy Place, London, W.C.2)—Convention on "Television and Film Techniques".

Thursday, April 20—Thursday, May 4

ENGINEERING, MARINE, WELDING AND NUCLEAR ENERGY EXHIBITION (at Olympia, London).*

Friday, April 21

SOCIETY OF CHEMICAL INDUSTRY, FINE CHEMICALS GROUP (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Annual General Meeting, 7 p.m.—Prof. F. Bergel, F.R.S.: "Newer Developments in Carcino-Chemotherapy".

INSTITUTION OF ELECTRONICS (in the Large Lecture Theatre, London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 7 p.m.—Mr. T. D. Towers: "Modern Transistors and Their Applications".

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

LECTURER IN MATHEMATICS—The Principal, Borough Road College, Isleworth, Middlesex (April 21).

ASSISTANT LECTURER IN PHYSICAL CHEMISTRY—The Registrar, The University, Hull (April 26).

ASSISTANT LECTURERS (2) (one with qualifications in the field of pure mathematics and the other with qualifications in the field of applied mathematics) IN THE DEPARTMENT OF MATHEMATICS—The Registrar, The University, Manchester 13 (April 27).

ASSISTANT LECTURER IN STATISTICS; a LECTURER or ASSISTANT LECTURER IN APPLIED MATHEMATICS; and a LECTURER IN PURE MATHEMATICS—The Registrar, The University, Sheffield (April 29).

ASSISTANT LECTURER or LECTURER IN PURE MATHEMATICS—The Registrar, University College, Singleton Park, Swansea (April 29).

DEMONSTRATOR IN THE DEPARTMENT OF GEOGRAPHY—The Registrar and Secretary, King's College (University of Durham), Newcastle upon Tyne 1 (April 29).

SENIOR LECTURER IN INORGANIC CHEMISTRY (Durban); and a LECTURER IN INORGANIC CHEMISTRY (Pietermaritzburg), University of Natal, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa and London, April 30).

ASSISTANT CHIEF GEOLOGIST (with an appropriate university degree (preferably with honours), together with wide geological experience in the investigation of sedimentary basins and particularly in exploration and development of oilfields) in the Bureau of Mineral Resources, Department of National Development, Commonwealth of Australia, to be responsible for the Bureau's sedimentary programme of geological investigation of the sedimentary basins of Australia; prepare advice on problems related to the search for oil; and to assist the Chief Geologist in technical and administrative matters—Official Secretary (Ref. 61/2083), Australia House, Strand, London, W.C.2 (May 1).

ASSISTANT DIRECTOR (with post-doctoral research experience, preferably in the application of the electron microscope and related physical methods in biology or medicine) OF RESEARCH IN THE ELECTRON MICROSCOPE SECTION of the Cavendish Laboratory—The Secretary of the Appointments Committee of the Faculty of Physics and Chemistry, Chemical Laboratory, The University, Lensfield Road, Cambridge (May 1).

LECTURER or ASSISTANT LECTURER (honours graduate in zoology or physiology) IN THE DEPARTMENT OF ZOOLOGY—The Registrar, The University, Leeds 2 (May 1).

LECTURER (with an honours degree in physiology or an allied subject, or equivalent training) IN THE DEPARTMENT OF PHYSIOLOGY—The Secretary, The University, Edinburgh (May 1).

LECTURER or ASSISTANT LECTURER IN THE DEPARTMENT OF ORGANIC CHEMISTRY—The Registrar, The University, Leeds 2 (May 5).

RESEARCH DEMONSTRATOR (with experience or interest in stratigraphy, structure and/or stratigraphical palæontology) IN THE DEPARTMENT OF GEOLOGY—The Registrar, University College of South Wales and Monmouthshire, Cardiff (May 5).

ASSISTANT LECTURER (preferably with interests in ecology, particularly its physiological aspects) IN BOTANY—The Registrar (Room 22, O.R.B.), The University, Reading (May 6).

DEMONSTRATORS (2) IN THE SCHOOL OF AGRICULTURE—The Registrar and Secretary, King's College (University of Durham), Newcastle upon Tyne 1 (May 6).

POSTDOCTORAL FELLOW IN THE DEPARTMENT OF CHEMISTRY, to carry out research into the reactions of halogen atoms with organic molecules, in collaboration with Dr. J. M. Tedder—The Registrar, The University, Sheffield 10 (May 6).

BURN RESEARCH FELLOW (graduate, less than 30 years old, with two to three years research experience) IN PHARMACOLOGY at Oxford—Secretary to the Trustees, Department of Pharmacology, University of Oxford (May 15).

DEMONSTRATOR IN BOTANY—The Registrar, The University of Adelaide, Adelaide, South Australia (May 15).

READER IN PHYSIOLOGY at the Royal Free Hospital School of Medicine—The Academic Registrar, University of London, Senate House, London, W.C.1 (May 18).

ASSISTANT LECTURERS IN APPLIED OR PURE MATHEMATICS at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong and London, May 19).

LECTURER (with a good honours degree in zoology, and preferably some experience of teaching and research) IN ZOOLOGY at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong and London, May 30).

CHAIR OF GEOGRAPHY in the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand and London, May 31).

LECTURER or ASSISTANT LECTURER (preferably candidate interested in genetics and ecology) IN ZOOLOGY—The Registrar, Pius XII College, Roma, Basutoland, Southern Africa (May 31).

CHAIR OF PHYSIOLOGY in Monash University, Clayton, Victoria, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, June 10).

ASSISTANT LECTURER IN INORGANIC CHEMISTRY—The Secretary, Queen Elizabeth College (University of London), Campden Hill Road, London, W.8.

PHYSICISTS AND CHEMISTS (with an honours degree or equivalent in physics or chemistry with at least three years relevant experience, or Associates of the Royal Institute of Chemistry) as Reactor Operating Staff at Dounreay Experimental Reactor Establishment, Thurso, Caithness, Scotland, to take control of a shift team responsible for the safe and efficient operation of the high flux Materials Testing Reactor, its ancillary plant and the experimental test rigs under irradiation in it—The Personnel Manager, D.E.R.E., U.K.A.E.A., Dounreay, Thurso, Caithness, Scotland, quoting Ref. 214/34.

PLANT PATHOLOGIST (male, aged between 28 and 45, with an honours degree in botany having specialized in mycology, together with at least two years postgraduate experience, and preferably experience in plant diseases in the tropics, especially diseases of cocoa) in Sierra Leone, to advise the Director of Agriculture on the application of phytosanitary measures and to undertake investigations into the control of plant diseases—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/15/019.

RESEARCH ASSISTANTS (graduates) IN THE DEPARTMENTS OF BOTANY AND ZOOLOGY, CHEMISTRY, MATHEMATICS, METALLURGY (GEOLOGY), AND PHYSICS—The Secretary, Sir John Cass College, Jewry Street, London, E.C.3.

RESEARCH ASSISTANTS (with a degree in chemistry or chemical engineering, or with equivalent qualifications such as Grad.R.I.C.) IN THE DEPARTMENT OF CHEMISTRY, for experimental work on the thermodynamic properties of gases and of liquid mixtures—The Bursar, The University, Reading.

SENIOR LECTURER (well qualified academically in mathematics, and preferably with industrial and teaching experience) IN MATHEMATICS—The Academic Registrar, Loughborough College of Technology, Loughborough, Leicestershire, quoting Ref. S.6.

SENIOR TECHNICIAN or TECHNICIAN IN THE CLINICAL ISOTOPE LABORATORY—The House Governor, St. Mary's Hospital, Paddington, London, W.2.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

The Reason for Studying Plant Diseases. By Prof. N. F. Robertson. (An Inaugural Lecture delivered in the University of Hull, 10 February, 1960.) Pp. 1+14. (Hull: The University, 1960.) 2*s.* 6*d.* [191

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 20: The Rearing of Chickens. Pp. 15. (Belfast: Ministry of Agriculture, 1960.) [191

Ordnance Survey. Map of Ilfracombe and District. (Sheet 86.) Scale: 1 : 25,000 (about 2½ inches to One Mile). (Chessington: Ordnance Survey, 1961.) Paper 6*s.* 6*d.* net. [191

Office of the Minister for Science. Scale of Enterprise in Farming: a Report by the Natural Resources (Technical) Committee. Pp. vi+110. (London: H.M. Stationery Office, 1961.) 6*s.* net. [191

Flora of Tropical East Africa. Edited by Dr. C. E. Hubbard and E. Milne-Redhead. Aizoaceae. By C. Jeffrey. (London: Crown Agents for Oversea Governments and Administrations, 1961.) 4*s.* [191

Society for Freedom in Science. Occasional Pamphlet No. 20: The Two Aspects of Science. By Sir George Thomson. Pp. 5. (Oxford: Assistant Secretary, Society for Freedom in Science, Department of Zoology, University Museum, 1960.) 1*s.* 3*d.* [191

Laboratory Animals Centre, Carshalton. Collected Papers, Vol. 9, 1960: Report of a Symposium on the Provision of Animals for Cancer Research, held at the Royal Society of Medicine, 23rd May, 1960. (Carshalton, Surrey: Laboratory Animals Centre, M.R.C. Laboratories, 1960.) 12*s.* 6*d.* [191

Johnson, Matthey and Co., Ltd. Publication No. 1302: Electrical Contacts. Pp. 30. (London: Johnson, Matthey and Co., Ltd., 1960.) [191

Manchester Public Libraries. The 108th Annual Report of the Libraries Committee, 1959–1960. Pp. 36+2 plates. (Manchester: Manchester Public Libraries, 1960.) [191

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WOOLWICH POLYTECHNIC

Principal: HAROLD HEYWOOD, D.Sc.Eng., Ph.D., A.C.G.I., Wh.Sch., M.I.Mech.E., M.I.Chem.E.

College of Engineering and Science
with Teachers Recognized by the UNIVERSITY OF LONDON

The College specializes in Advanced Studies and Research. The Degree Courses are conducted under Teachers recognized by the University of London. The Courses for the Diploma in Technology are approved by the National Council for Technological Awards. In the past few years the College has been recruiting full-time students on an increasing scale for Advanced Studies and Research and the number of full-time students reading for Degrees, Diplomas in Technology and in courses leading thereto now exceeds 800. Large extensions are now being erected to enable the College to meet the increasing demand for places.

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B.Sc. Special in Mathematics.
B.Sc. Special in Physics.
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AND INDUSTRIAL ADMINISTRATION
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The Warden, The College of Aeronautics, Cranfield, Bletchley, Bucks

APPOINTMENTS VACANT

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A. UNDERWATER WEAPONS ESTABLISHMENT, PORTLAND, DORSET (Ref. C69/1A)

(1) Mechanical Engineer. Specialized in thermodynamics with experience in internal combustion engine research and/or rocket propulsion field. Minimum five years' experience in either expected. Some experience in appropriate instrumentation essential with design study work on components of rocket systems or other propulsion gear. Turbine design experience advantageous.

(2) Mechanical Engineer with bias for one or more of: (i) hydraulically operated mechanisms, including servo-control; (ii) mechanics of machines (theory and practice); (iii) hydro- (or aero-) dynamics of fairly elementary character.

(3) Hydrodynamicist (or aeronautical engineer), with some years' experience for work on torpedo dynamics.

(4) Mechanical Engineers (servo-mechanisms, gyro design and develop). Electrical Engineers (Electronics/Design). Mathematicians (Operational research and theoretical physics). Physicist (acoustics).

B. GOVERNMENT COMMUNICATIONS H.Q., CHELTENHAM (Ref. A43/1A)

Physicists (Telecommunications). Mathematicians. Electrical Engineers (Electronics/Radar: Telecommunications and Radio).

C. NAVAL CONSTRUCTION RESEARCH ESTABLISHMENT, DUNFERMLINE (Ref. C70/1A)

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D. ADMIRALTY COMPASS OBSERVATORY, SLOUGH (Ref. D47/1A)

Electrical or Mechanical Engineers or Physicists interested in gyro-techniques, servo-mechanisms or electronics.

Qualifications for all posts first- or second-class honours degree or equivalent in appropriate subject. Must normally be natural born British subjects of natural born British parents. Senior Scientific Officers must have had minimum three years' postgraduate experience and be not less than 26 years of age.

Salaries: (A.) Senior Scientific Officer, £1,302 to £1,604; Scientific Officer, £717 to £1,186. (B. C. D.) Senior Scientific Officer, £1,342 to £1,654; Scientific Officer, £738 to £1,222.

Appointments unestablished (with F.S.S.U. benefits) but opportunities for those between 21 and 32 to compete for established posts.

Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting appropriate reference and post.

CENTRAL ELECTRICITY GENERATING BOARD

EASTERN DIVISION

Applications are invited from Mathematicians for the following appointment:

MATHEMATICAL ASSISTANT

BRADWELL (NUCLEAR) GENERATING STATION (ESSEX)

Salary range £670 to £805 per annum.

The commencing salary will depend upon age and qualifications.

The work will be varied in nature, involving analysis and calculations based on physical measurements made on the nuclear reactors, in order to ensure their safe and efficient operation.

Opportunities to write programmes for a large, modern computer (I.B.M.709) will arise, and a period of training for this type of work will be provided.

Applications, quoting Reference No. S.V.1417, stating age, details of education, experience and present position, should be sent to the Controller, Central Electricity Generating Board, Eastern Division, West Farm Place, Chalk Lane, Cockfosters, Barnet, Herts, by April 22, 1961.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

FRUIT RESEARCH OFFICER (PHYSIOLOGIST)

The Organization's Division of Food Preservation invites applications for appointment as Fruit Research Officer (Physiologist) at the new headquarters laboratories, North Ryde, Sydney, N.S.W.

The Fresh Fruit Storage Section, which co-operates closely with the Plant Physiology Research Unit of the Division, and University, is engaged on studies related to the development, ripening and senescence of fruits. The appointee is required to participate in a programme of physiological and biochemical investigations to obtain a better understanding of the ripening of fruit and its behaviour in storage.

Applicants should be honours graduates in science or agricultural science (or equivalent qualifications) with relevant postgraduate research experience, preferably in plant physiology or biochemistry.

Salary: Dependent on qualifications and experience within the range £A.1,510 to £A.2,265 per annum.

Salary for a woman will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the range within which the original appointment is made.

Fares paid. Further particulars supplied on application to:

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2.

to whom applications (quoting Appointment No. 300/298) should be addressed by May 20, 1961.

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ANIMAL HOUSE TECHNICIANS. SEVERAL vacancies exist in different grades for work with laboratory animals. Commencing salaries according to age, educational qualifications, and previous experience.—Applications should be made in writing to the Administrative Officer, NUTRITIONAL RESEARCH UNIT, HUNTINGDON.

PHYSIOLOGIST, LECTURER, DEPARTMENT of Physiology, University of Ottawa, Ottawa, Canada. Applicants should have an M.D. or a Ph.D. degree. Salary up to $6,000, depending on experience. Pension plan, hospital insurance.—Applications and inquiries should be forwarded to Professor M. Beznak at the above address.

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for work associated with the design and development of the latest Ferranti range of digital computers.

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* **Applications should be made in writing to T. J. Lunt, Staff Manager, Ferranti Limited, Hollinwood, Lancs, giving brief details of qualifications and experience. Please quote reference KLD.**

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The Personnel Manager,
British Titan Products Company Limited,
Billingham, Co. Durham,
quoting reference S.7.

ROYAL HOLLOWAY COLLEGE
(UNIVERSITY OF LONDON)
ASSISTANT LECTURESHIP IN BOTANY

The Council invites applications for the post of Assistant Lecturer in Botany, tenable from October 1, 1961. An interest in mycology is desirable. The post is open to a man or a woman; women are usually expected to be resident. The salary will be on the scale approved by the Senate of the University of London, according to experience.

Particulars may be obtained from the Principal, Royal Holloway College, Englefield Green, Surrey, to whom applications should be sent not later than May 8, 1961.

WOOLWICH POLYTECHNIC
LONDON, S.E.18

Principal: Harold Heywood, D.Sc., Ph.D., A.C.G.I., Wh.Sch., M.I.Mech.E., M.I.Chem.E.

Applications invited for Assistant Lecturer, Grade B, in Physics to teach in the first instance up to General Certificate of Education, "A" level, and Part I B.Sc. General Degree. The Physics Department includes classes for students taking Internal degrees of B.Sc. Special Physics and B.Sc. General of the University of London. Salary within £828 to £1,426, according to qualifications and experience.

Particulars and application form from Clerk to the Governors, to be returned by April 29, 1961.

AUSTRALIAN NATIONAL UNIVERSITY

Applications are invited for the following appointments, all of which are new posts, in the School of General Studies of the University. Appointees will be required to take up duty on January 1, 1962, or as soon as possible thereafter.

FACULTY OF ARTS

Senior Lecturer or Lecturer in Pure Mathematics.

FACULTY OF SCIENCE

Lecturer in Chemistry; Senior Lecturer or Lecturer in Genetics; Senior Lecturer or Lecturer in Geology; Lecturer in Physics; Lecturer in Electronics. Senior Lecturer or Lecturer in Zoology; Lecturer or Senior Demonstrator in Zoology.

Salary ranges: Academic salaries are under revision. At present the ranges are as follows: Senior Lecturer, £A.2,400 by £A.100 to £A.2,900; Lecturer, £A.1,640 by £A.90 to £A.2,360; Senior Demonstrator, £A.1,430 by 3 by £A.50 by 1 by £A.60 to £A.1,640. Commencing salary will be in accordance with qualifications and experience.

Further information and the summary forms which must accompany an application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 20, 1961.

NATIONAL PHYSICAL LABORATORY (D.S.I.R.), Teddington, Middlesex, requires Senior/Scientific Officers in: Applied Physics Division, (1) Electrical Engineer or Physicist with electricity bias, for development of greater accuracy in electrical measurements and instruments. Strong interest in precision measurement and research on industrial experience desirable. (Ref. D.170/1A.) (2) Radiochemist for general work in Radiology Section with particular interest in problems arising in standardization of very dilute solutions. (Ref. F.365/OA). Qualifications: first- or second-class honours or equivalent. Minimum three years postgraduate experience for Senior Scientific Officer minimum age 26. Salary ranges: Scientific Officer, £773 to £1,267; Senior Scientific Officer, £1,392 to £1,714. Appointments unestablished initially.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting appropriate reference.

LABORATORY TECHNICIAN

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Rapidly expanding Radioisotope Department

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Halifax, Nova Scotia

QUALIFICATIONS: Good background of Hematological and Allied Laboratory Technique, preferably one "A" level science subject.

Pleasant working conditions, full Civil Service Benefits.

SALARY RANGE: Commensurate with qualifications and experience.

For further details apply to Dr. J. E. Stapleton, Radiotherapy Department, Victoria General Hospital, Halifax, Nova Scotia.

Application forms may be obtained from the Nova Scotia Civil Service Commission, P.O. Box 943, Provincial Administration Building, Halifax, Nova Scotia.

Applications are invited from honours graduates for the post of

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The work will be mainly in the field of polymer chemistry, although most branches of Physical Chemistry will be covered. The Passfield Research Laboratories are newly built in pleasant rural surroundings and are well equipped with up-to-date instruments.

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Write in confidence to:

The Director of Research,
Passfield Research Laboratories,
Passfield, Liphook, Hampshire

HONG KONG

Scientific Officer (Medical) who would be responsible to the Government Pathologist, required for work in Biochemistry Section of Government Institute of Pathology and for duties connected with training of technologists. Candidates must possess honours degree in science (biochemistry) of a British university and have had one year's postgraduate experience in a hospital clinical biochemistry laboratory. Appointment on permanent basis with pension (non-contributory). Salary scale £1,350 to £2,865 per annum. Income tax at local rates. Government quarters normally provided at nominal rental. Passages for officer, wife and children not exceeding five passages in all.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD.117/51/056).

DALHOUSIE UNIVERSITY

HALIFAX, NOVA SCOTIA, CANADA

As part of an expansion programme applications are invited for the following positions:

Assistant Professor in Microanatomy to teach medical and science students and conduct research in embryology. Preference will be given to candidates with a science degree in zoology or medical qualification.

Assistant Professor in Gross Anatomy primarily to teach gross anatomy, with opportunities to participate in research and in other responsibilities of the department. Modern facilities for research available. The salary for an Assistant Professor with medical qualifications will be not less than $8,500, depending upon qualification.

Inquiries for both appointments should be addressed to Professor R. L. de C. H. Saunders at Canada House, London, England.

AIR MINISTRY

SCIENTIFIC ADVISER'S DEPARTMENT

Air Ministry require unestablished Senior Scientific, Scientific Officer and Experimental Officers in Scientific Adviser's Department.

Qualifications: Senior Scientific and Scientific Officers should have first- or second-class honours degree in one of the subjects specified. Experimental Officers should be between 26 and 31, and have pass degree, H.N.C. or G.C.E. "A" Level including at least one of the subjects specified.

Four Scientific Officer posts at A.M. Headquarters Whitehall for Graduates in Mathematics or Physics.

Post A—in Strategic Offence and Atomic Section, involving cost/effectiveness studies of offensive systems, studies on strategy of R.A.F. offensive operations, and of atomic effects and target response. Mathematician preferred.

Post B—in Air Defence and Electronics Section involving cost/effectiveness studies of defensive systems and detailed electronic studies of radar, electronic counter-measures, and infra-red. Physicist preferred.

Post C—in Strategic Studies and Anti-submarine Warfare Section, involving studies of interplay of offence and defence, and the requirements of nuclear submarine detection.

Post D—in Limited War Section involving studies of tactical aircraft, tactical weapons systems and limited form of war games in tactical sphere.

Three Senior Scientific or Scientific Officer posts on staff of Operational Research Branch at Bomber Command, High Wycombe, for Graduates in Mathematics, Physics or Engineering.

Post E—at Command H.Q. involving work on evaluation, use and operation of airborne and ground electronic equipment. Good electronics background required, preferably with experience on airborne and ground radar.

Post F—at Command H.Q. involving work on problems of effectiveness of Medium Bomber Force and in programming and organization of an Elliott 402 computer. Good mathematical background required.

Post G—involving work on trials of Bluesteel and also work at Bomber Command Development Unit at Finningley, Yorks.

Two Experimental Officers for Post H—at H.Q. Bomber Command, High Wycombe, to assist in computer programming to train other programmers and to participate in work involving bombing calculations, defect recording systems, nuclear fallout profiles, etc. Be interested in problems of data handling and have qualifications in mathematics, physics or engineering.

Post I—at H.Q. Technical Training Command, Brampton, Hunts, concerned with collection and analyses of data, and conducting experiments in training of technicians. Background and qualifications in social sciences with some knowledge of statistics preferred but qualifications and experience in electronic engineering acceptable.

Salaries, National rate: Senior Scientific Officers, £1,342 to £1,654; Scientific Officers, £738 to £1,222; Experimental Officers, £1,087 to £1,336, £55 to £65 more for posts in London.

Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1. (Quoting A 128/1A and appropriate Post ref.)

SCOTTISH PLANT BREEDING STATION

ECOLOGIST

Applications are invited for the post of ecologist in the Genecological Section of the Station. Preference given to applicants interested in the physiological bases of plant adaptation to environment, and who are willing to co-operate in the present programme concerned with hill-land communities. An honours degree is a minimum requirement. Starting salary in accordance with experience and age within the range: Scientific Officer, £738 to £1,222; Senior Scientific Officer, £1,342 to £1,654. Participation in F.S.S.U.

Applications, accompanied by the names of three referees, should be sent to the Secretary, Scottish Plant Breeding Station, Pentlandfield, Roslin, Midlothian, before May 6, 1961.

UNIVERSITY COLLEGE, DUBLIN

PROFESSORSHIP OF ORGANIC CHEMISTRY

Applications are invited by the Governing Body of University College, Dublin, for the above Statutory Office. Applicants must forward to the Secretary and Bursar, University College, Dublin, 150 copies of their applications and testimonials, to be received by him not later than May 15, 1961.

Further particulars may be obtained from

J. P. MacHALE,
Secretary and Bursar.

University College,
Earlsfort Terrace, Dublin.

MONASH UNIVERSITY
CLAYTON, VICTORIA, AUSTRALIA
CHAIR OF MEDICAL BIOCHEMISTRY

The Interim Council of Monash University invites applications to the Foundation Chair of Medical Biochemistry. The University opened on March 13, 1961, with Faculties of Medicine, Arts, Economics and Politics, Science and Engineering, at Clayton, 14 miles from the centre of Melbourne. Students who began the first year of their medical course in March, 1961, will start Medical Biochemistry in March, 1962. Planning for the first portion of the Medical School to be built by the end of 1962 is proceeding, and multi-discipline laboratories for Medical Biochemistry, Physiology, Pharmacology and Histology will be incorporated. Biochemistry, other than Medical, will be taught in the Chemistry School. The successful applicant will have the opportunity to take part in the planning of his department, and, if from overseas, air fares will be paid for this purpose so that, immediately on appointment, a short visit for consultation with the Dean of the Faculty and the Architects can take place. For the building of the first phase (1961-63) of the Medical School (Anatomy, Medical Biochemistry and Physiology) the Australian Universities Commission has allotted £500,000. The first three years of the course will be at the University, and the three clinical years at Alfred Hospital (with its associated Baker Medical Research Institute) and Prince Henry's Hospital. The Chairs of Pathology and Microbiology will be at Alfred Hospital and the Clinical Chairs at the two hospitals. A site next to the Medical School has been reserved at the University for a General Teaching Hospital which, it is expected, will be built in the next ten years. The successful applicant will be a full-time officer of the University and will be expected (i) to teach, conduct examinations and exercise supervision over the work of his Department in accordance with the University Statutes and Regulations and the direction of the Interim Council to whom he will be responsible through the Vice-Chancellor, (ii) to carry out and organize research amongst staff and postgraduate students and (iii) to advise the Interim Council on the establishment and development of his own Department. The salary of the Professor will be subject to negotiation, but will be not less than £A.4,000 per annum. Superannuation provision is similar to F.S.S.U.; there will be travelling and removal expenses to Melbourne for the appointee and his family.

Further information and details of the terms and conditions of appointment for the Chair may be obtained from the undersigned, with whom applications close on June 10, 1961, or from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1.

F. H. JOHNSON,
Registrar.

Monash University,
Clayton, Victoria, Australia.

PLANT PATHOLOGIST
SIERRA LEONE

To advise the Director of Agriculture on the application of phytosanitary measures and to undertake investigations into the control of plant diseases. Candidates (male), aged between 28 to 45, must have an honours degree in botany having specialized in mycology, together with at least two years' postgraduate experience. Experience in plant diseases in the tropics, especially diseases of cocoa, desirable. Appointment on contract/gratuity terms for two tours of 15 to 18 months in the first instance. Salary, including inducement pay, in scale £992 to £1,924. Gratuity 15 per cent of aggregate gross salary. Free passages on appointment and leave for officer, wife and up to three dependent children under 18 years of age. Furnished quarters, usually available, at low rental. Generous leave.

Apply, stating full name and giving brief particulars of qualifications and experience, to Director of Recruitment, Colonial Office, London, S.W.1. Quote BCD.63/15/019/C1.

UNIVERSITY OF NOTTINGHAM

Applications are invited for the appointment of Lecturer in Electrical Engineering. Candidates should preferably, though not necessarily, have had some industrial experience and be interested in teaching and research in one or more of the following fields: Electrical Machines; Electrical Power; Computers; Electronics. Salary scale £1,050 to £1,850, initial salary according to qualifications and experience, with membership of the Universities' Superannuation Scheme and children's allowance.

Conditions of appointment and form of application, to be returned by May 5, 1961, from the Registrar.

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The training salary for the first two years is £793 and £824. On satisfactory completion the scale is £941–£1,719 by regular increments, but there is a jump in the scale to £1,324 five years after entry, or only four or even three in cases of special merit. Approved postgraduate experience fetches a higher starting salary. One promotion only, of which prospects are excellent, raises your maximum to £2,715. Reasonable proportion of still higher posts up to £3,865 all filled exclusively by promotions from entry grade.

qualifications

Age 21–35 and first- or second-class honours degree in physics, chemistry, engineering or mathematics, or an equivalent such as A.R.I.C., A.Inst.P., or corporate membership of I.C.E., I.Mech.E., or I.E.E., or first- or second-class honours Diploma of Technology.

conditions

Location, London, five-day week. Annual leave 4½ rising to 6 weeks. Posts are permanent and pensionable (non-contributory).

Write or telephone for further information, or for a visit to the Patent Office to see the work, entirely without obligation. **The Superintending Examiner (B Staff), The Patent Office, 25 Southampton Buildings, London, W.C.2. Telephone** HOLBORN 8721. **Ext.** 324.

SENIOR ORGANIC CHEMISTS

required by TEXACO TRINIDAD, INC.

for service in TRINIDAD

Applicants should have a Ph.D. degree and, unless their research career has been particularly relevant, two or three years industrial experience. Their work will be concerned with the production of organic chemicals from petroleum hydrocarbons. Commencing salary depending on experience will be in the region of £1,600 per annum, and suitable candidates may be considered for promotion to Group Leader after about one year.

Texaco Trinidad, Inc. provides cheap accommodation for married and single men, excellent clubs and facilities for a wide range of sports, comprehensive medical arrangements, schooling for children up to the age of 16, and a good pension scheme.

Applicants who have the required qualifications and experience are invited to write for an application form to:

The Personnel Officer, Trinoil (U.K.) Limited,
29/30 Old Burlington Street, London, W.1.

AUSTRALIA

COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION

RESEARCH BOTANIST

(No. 290/594)

The Organization's Division of Forest Products, Melbourne, Victoria, invites applications from Honours graduates in Science or Agricultural Science, majoring in Botany (or equivalent qualifications), for the position of Research Botanist in the Wood and Fibre Structure Section.

The Division's research is concerned with fundamental data on the properties, potentialities, and correct methods of treatment of Australian timbers and provides assistance to all concerned in the use of timber. The appointee will undertake research within this programme either on :

(a) cell wall and cytoplasmic structure, using optical techniques and electron microscopy, for which additional training to degree level in chemistry or physics is desired ; or

(b) anatomical and physiological changes associated with the ageing of meristems, and studies of the estimation and distribution of enzymes and differentiating tissues for which training to degree level in plant physiology or biochemistry would be an advantage.

PLANT PHYSIOLOGIST OR BIOCHEMIST

(No. 300/303)

The Organization's Division of Food Preservation invites applications for appointment as Plant Physiologist or Biochemist at the Plant Physiology Unit, located in the Botany Department, University of Sydney. The Unit, operated jointly by the Division and the University, conducts research in the physiology, biophysics and biochemistry of plant tissues.

Applicants should be Honours graduates in Science, majoring in Botany or Biochemistry (or equivalent qualifications), with post-graduate research experience in plant physiology or biochemistry.

Salary : dependent on qualifications and experience within the ranges £A.1,510 to £A.2,265 per annum or £A.2,395 to £A.2,720 per annum.

Salary for a woman will be £A.180 per annum less than corresponding rates for men.

Promotion within C.S.I.R.O. is by merit and may ultimately go beyond the upper limit of the range within which the original appointment is made.

Fares paid. Further particulars supplied on application to :

Mr. E. J. Drake, Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2,

to whom applications (quoting relevant Appointment number) should be addressed by May 20, 1961.

PRODUCTS APPLICATION

As a result of continuing expansion, a

PHYSICIST

with a good honours degree, postgraduate, academic or industrial training in laboratory techniques, preferably concerned with optics and lighting, is required to supervise the building and calibration of an artificial sky and to carry out model experiments.

Apply to the **Personnel Officer (Graduate Recruitment),**

PILKINGTON BROTHERS LIMITED,

Glass Manufacturers,

ST. HELENS, Lancs

ONTARIO CANCER FOUNDATION

HAMILTON CLINIC
HAMILTON GENERAL HOSPITAL,
HAMILTON, ONTARIO

Applications are invited for appointment as Clinical Physicist. Applicants should possess at least an honours degree in physics or equivalent. Some experience in hospital physics is desirable but not necessary. An interest in research in clinical physics or radiobiology is expected. Minimum initial salary for untrained honours graduate is $5,000 per annum ; pension scheme.

Applications should be sent to the undersigned, from whom further details may be obtained.

R. J. HORSLEY,
Senior Physicist.

UNIVERSITY OF BRITISH COLUMBIA

Invites applications for the post of
ASSISTANT PROFESSOR OF METALLURGY

Attractive post in expanding Department for a man in the field of physical metallurgy, metal physics, materials science. Applicants should have Ph.D. or equivalent and subsequent academic, industrial, or research experience. Duties comprise undergraduate teaching, supervision of graduate work and participation in research at professional level. Opening available September 1, 1961. Salary $7,000 per year plus generous benefits.

Applications should be submitted by June 30 next, to Professor F. A. Forward, Head of the Department, University of British Columbia, Vancouver 8, B.C.

SUNDERLAND EDUCATION AUTHORITY

TECHNICAL COLLEGE

DEPARTMENT OF CHEMISTRY AND BIOLOGY

Applications are invited for the following posts which arise from expansion of the work of the Department :

(a) **Lecturer in Applied Chemistry,** to teach the subject in courses leading to the degree in Applied Science of the University of Durham, Higher National Diplomas in Engineering, and Diplomas in Technology. A degree and/or professional qualifications with appropriate industrial, research, or teaching experience essential.

(b) **Lecturer in Inorganic Chemistry,** to teach to the standard of Honours Degree and Grad.R.I.C. Good honours degree essential ; an active interest in research, together with teaching experience would be an advantage.

Both research and collaboration with industry are encouraged. Salary scale (Burnham Technical Report, 1959) :

£1,370 by £35 to £1,550.

The Education Authority is prepared to help successful candidates with removal expenses, lodging allowance, and house purchase.

Further particulars of the above posts may be obtained from the Registrar, Technical College, Sunderland, Co. Durham. Completed applications should be sent to the undersigned within fourteen days of the appearance of this advertisement. Canvassing disqualifies.

W. THOMPSON,
Director of Education.

Education Offices,
15 John Street, Sunderland.

AUSTRALIAN NATIONAL UNIVERSITY

SENIOR LECTURER IN PSYCHOLOGY
SENIOR DEMONSTRATOR IN PSYCHOLOGY

Applications are invited for two positions of Senior Lecturer and Senior Demonstrator in the Department of Psychology in the School of General Studies. Appointees will be required to take up duty on January 1, 1962, or as soon as possible thereafter. Applicants for the Senior Lectureship must possess a higher degree in psychology or equivalent qualifications, and be interested in pursuing research. It is desirable that applicants should have had research and specialist experience in social psychology (including group dynamics), personality or behaviour theory ; and experience in teaching general or social psychology. Applicants for the Senior Demonstratorship should be honours graduates who are already pursuing, or have plans to pursue, work for the Ph.D. degree in Psychology. The field is open, but preference may be given to a candidate whose special interest lies in either experimental psychology, personality assessment or experimental social psychology. The salary range for a Senior Lecturer is £A.2,400 to £A.2,900 ; and for a Senior Demonstrator £A.1,430 to £A.1,640. Commencing salary will be in accordance with qualifications and experience.

Further information will be supplied on request to the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1, with whom two copies of each application must be lodged. Two further copies of applications, giving the names of three referees and including details of academic qualifications, teaching experience and research interests, should be forwarded to the Registrar, School of General Studies, Australian National University, P.O. Box 197, Canberra City, A.C.T., Australia, with whom applications close on June 24, 1961.

C. G. PLOWMAN,
Acting Registrar, School of General Studies.

FORDHAM UNIVERSITY

NEW YORK CITY
DEPARTMENT OF CHEMISTRY
RESEARCH ASSISTANTSHIP

For the study of high pressure solubility of gases in salt solutions. Geochemical implications. Prefer student working toward the Ph.D. $200/month.

Apply to : Dr. Norman O. Smith
Department of Chemistry
Fordham University
New York 58, N.Y., U.S.A.

There is a vacancy in the Biological Research Department of GLAXO LABORATORIES LTD., Greenford, Middlesex, for a

Senior Graduate

in a biological science to take charge of a section engaged in the preparation of an immunological product.

The post is suitable for someone in his early thirties who has four or five years' post-graduate experience and the ability to administer a staff of about 10. Applications are invited from graduates in an appropriate biological science who have a knowledge of bacteriology. The processes involve the extensive use of freeze-drying and some knowledge in this field and or some mechanical aptitude would be an advantage.

The successful applicant will be encouraged to undertake a certain amount of research work and full facilities for this will be provided.

An attractive salary related to age and experience will be offered to the successful candidate. The terms of service are generous and include a Pension Scheme, and the opportunity to participate in the Company's profitability.

Apply to the Personnel Manager, Glaxo Laboratories Ltd., Greenford, Middlesex.

PRESSED STEEL COMPANY LIMITED

With the expansion of Research and Development within Pressed Steel, the Company now wishes to appoint a:

LIBRARIAN

who will assist in the building up of the Information Section in the Research and Development Department. Initially the work will be mainly cataloguing, but there will be opportunities for advancement in an expanding section.

Applications are invited from Librarians (Chartered) with sound cataloguing and other experience, preferably in a special or technical library. A knowledge of languages and a technical background would represent an attractive attainment. The appointment will be to the permanent staff and will carry a salary commensurate with experience.

Write in strict confidence, giving full details of education, training, experience, and salaries earned to the Staff Officer, Pressed Steel Company Limited, Cowley, Oxford.

RESEARCH CHEMISTS

ICI

ORGANIC AND PHYSICAL CHEMISTS

are required by

PLANT PROTECTION LIMITED

(a subsidiary of IMPERIAL CHEMICAL INDUSTRIES LIMITED)

at its Research and Development Station

at JEALOTT'S HILL, near BRACKNELL, BERKSHIRE,

to investigate the synthesis and properties of new biologically active chemicals for use in Crop Protection. Applicants should possess good honours degrees in chemistry and postgraduate experience either at a university or in industry.

They should not exceed 30 years of age and should write in the first instance, giving brief particulars only, to the **Staff Officer, Plant Protection Limited, Fernhurst, near Haslemere, Surrey.**

SURREY EDUCATION COMMITTEE

KINGSTON TECHNICAL COLLEGE
FASSETT ROAD, KINGSTON-UPON-THAMES

Required September 1, 1961:

DEPARTMENT OF CHEMISTRY, BIOLOGY AND GEOLOGY

Lecturer in Inorganic Chemistry. Assistant Grade B in Geology with special qualifications in Stratigraphy and Sedimentation. Two Assistants Grade B in Chemistry. Assistant Grade B in Geography.

DEPARTMENT OF PHYSICS AND MATHEMATICS

Senior Lecturer in Mathematics. Lecturer or Assistant Grade B in Mathematics. Lecturer or Assistant Grade B in Physics.

Must be honours graduates, preferably with teaching or research experience. Salary, Burnham Technical Scale: Senior Lecturer, £1,550 by £50 to £1,750; Lecturer, £1,370 by £35 (4)/£40 to £1,550. Assistant, Grade B, £700 by £27 10s. (15)/£37 10s. to £1,150, plus London allowance.

Application forms and further particulars from Principal, to be returned as soon as possible, in any case not later than May 1, 1961.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF MATHEMATICS

Applications are invited for the post of Reader in Applied Mathematics. Salary scale: £1,800 by £50 to £2,100 per annum, plus London allowance of £38 or £51 according to age.

Information about the Department, together with further particulars of the post, may be obtained from the Clerk to the Governors. Applications by May 5, 1961.

UNIVERSITY OF BELFAST

The Senate of the Queen's University of Belfast invites applications for a lectureship in botany from September 1, 1961. Candidates are required to have a special interest in mycology, plant pathology or cognate subjects. Salary range £1,050 to £1,850, plus contributory pension rights under the F.S.S.U. Initial placing on the salary scale will depend on qualifications and experience. Applications should be received by May 10, 1961.

Further particulars may be obtained from G. R. Cowie, M.A., LL.B., J.P., The Secretary, The Queen's University of Belfast, Belfast 7, Northern Ireland.

UNIVERSITY OF LIVERPOOL

Applications are invited for the post of Lecturer in Veterinary Histology in the Department of Veterinary Anatomy. The initial salary will be within the range £1,050 to £1,400 per annum, according to age, qualifications and experience.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than May 31, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Quoting Reference CV/N.

NORTHERN POLYTECHNIC

HOLLOWAY, LONDON, N.7

The Governing Body invites applications for appointment as Senior Lecturer in Physics to commence in September, 1961. The work of the Department includes courses for the B.Sc. Special Degree (Internal of London University) and for the Dip.Tech. in Physics and post-graduate studies. Applicants should be qualified to direct research. Burnham Scale salary—at present £1,550 by £50 to £1,750, plus London allowance.

Apply for further particulars and form of application.

R. H. CURRELL, F.C.A.,
Clerk.

UNIVERSITY OF ST. ANDREWS

Applications are invited for a Lectureship in Pharmacology in the Department of Pharmacology and Therapeutics, Queen's College, Dundee, with effect from a date to be arranged. Salary scale: medically qualified, £1,050 by £100 to £2,000 (efficiency bar £1,450); non-medically qualified, £1,050 by £50 to £1,400 (efficiency bar) by £75 to £1,850. Placing on appropriate scale according to qualifications and experience but at a stage below the efficiency bar. Preference will be given to applicants possessing postgraduate science degrees in Pharmacology. F.S.S.U.; Family Allowance; Grant towards furniture removal expenses.

Applications (six copies), containing the names of three referees, to the undernoted within three weeks of the appearance of this advertisement.

PATRICK CUMMING,
Joint Clerk to the University Court.
Queen's College, Dundee.

UNIVERSITY OF NOTTINGHAM

Technician required for the Pharmacy Department. Applicants should have experience in laboratory work and a special interest in the construction and repair of laboratory apparatus. Salary within the scale £490 to £675.

Conditions of appointment and forms of application from the Registrar.

U.K.A.E.A.

NEUTRON PHYSICS RESEARCH

Physicists, with or without direct experience, are invited to apply for positions in the Nuclear Research Division at Aldermaston in one of the following research areas:

REACTOR PHYSICS

(including the physics of pulsed reactors)

NEUTRON SPECTROMETRY

Fundamental Physics of Neutron Interactions with Nuclei

The excellent experimental facilities available include two low power reactors specially designed for research in reactor physics, a 5 MW. research reactor equipped with time-of-flight systems for neutron physics studies, and two high voltage accelerators used as neutron sources.

Suitable applicants, who should have a good honours degree, will be invited to visit the laboratories and discuss the work with senior scientific staff.

Salary : £790 to £2,590 per annum, according to age, qualifications and experience.

Superannuation scheme. A house or substantial assistance with house purchase will become available for married officers living beyond daily travelling distance.

For further details please write to the Senior Recruitment Officer, A.W.R.E., Aldermaston, Berks, quoting ref. 2937/34.

SHELL

"SHELL" RESEARCH LIMITED

TUNSTALL LABORATORY

(Sittingbourne, Kent)

DIVISION OF PATHOLOGY

AN EXPERIMENTAL PATHOLOGIST

preferably with a medical qualification, is required to work in the Division of Pathology of this Laboratory. The programme of work is concerned with the structural changes of mammals resulting from chemical intoxication, the definition of latent anatomic change through the techniques of histochemistry and the investigation of tissue enzymes.

Salary in accordance with age, qualifications and experience. Five-day week, staff restaurant, excellent pension scheme. Please write giving details of qualifications and experience to:

Personnel Recruitment/E.P.,
"Shell" Research Limited,
St. Helen's Court,
Great St. Helen's,
London, E.C.3.

WEST OF SCOTLAND AGRICULTURAL COLLEGE

Applications are invited for a post of Lecturer in Botany from Graduates in Science with special qualifications in botany or agricultural botany (although intending graduates are not debarred from applying). The salary scale, which will depend on the age, qualifications and experience of the successful applicant, will be on one or other of the following grades: Grade III (Provincial), £975 rising to £1,570. Grade IV (Provincial), £698 (Honours Graduates £717) rising to £993.

Conditions of appointment and application forms are obtainable from the Secretary, 6 Blythswood Square, Glasgow, C.2, with whom applications should be lodged not later than April 24, 1961.

MECHANICAL ENGINEER FOR MINISTRY of Aviation at National Gas Turbine Establishment, Pyestock, nr. Farnborough, Hants, for research in turbo-machinery, great scope for analysing and rationalizing experimental and theoretical data. Appointment as Senior Scientific Officer (minimum age 26). First- or second-class honours in mechanical engineering (or equivalent qualification) and minimum three years' postgraduate research experience required; experience in turbines and/or compressors essential. Salary range £1,302 to £1,604 with superannuation under F.S.S.U. Opportunity for candidates under 31 (normally) to compete for established (non-contributory pensionable) posts. Early possibility of house to rent for married man.—Form from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting C.241/1A.

SUNDERLAND EDUCATION AUTHORITY

THE TECHNICAL COLLEGE

Applications are invited for the post of Lecturer and Senior Lecturer in the Physics Department. Duties to commence September 1, 1961. Salaries will be in accordance with the Burnham Scale: (a) Lecturer, £1,370 by £35 to £1,550 per annum; (b) Senior Lecturer, £1,550 by £50 to £1,750 per annum. Candidates must be well qualified and preference will be given to those who have had teaching, industrial and research experience. The Authority is prepared to help the successful candidate with removal expenses, lodging allowance and house purchase.

Further particulars and forms of application may be obtained from the Registrar, the Technical College, Sunderland, Co. Durham, and applications should reach the undersigned as soon as possible after the appearance of this advertisement. Canvassing disqualifies.

W. THOMPSON,
Director of Education.

15 John Street,
Sunderland, Co. Durham.

HANNAH DAIRY RESEARCH INSTITUTE

Physiologist, Zoologist or Veterinarian required for a post in the Physiology Department. The work is concerned with the basic physiology of temperature regulation in farm animals; excellent research facilities are available. The post offers much scope for original work in a wide field of investigation. Previous research experience in this field is not essential. Applicants should have a first- or second-class honours degree, preferably with a Ph.D., or a veterinary qualification with postgraduate research experience, but applications will be considered from candidates without postgraduate experience. The appointment will be made in the grade of Scientific Officer (£717 to £1,186) or Senior Scientific Officer (£1,302 to £1,604) according to experience and qualifications. F.S.S.U. Facilities exist to register for a higher degree.

Applications, naming three referees, to the Secretary, The Hannah Dairy Research Institute, Kirkhill, Ayr, by May 6, 1961.

MONASH UNIVERSITY

CLAYTON, VICTORIA, AUSTRALIA

VERTEBRATE PALAEONTOLOGIST; ETHOLOGIST

Applications are invited for the above-mentioned posts in the Department of Zoology. The Head of the Department is Professor A. J. Marshall, D.Phil., D.Sc.(Oxon). The appointments will be made at either Lectureship or Senior Lectureship level, depending on the status of the successful applicants. Both posts offer special opportunities for field work. The successful applicant in each case must be capable of giving an honours course and supervising research students in his subject. He would begin duties at some date before March, 1962. Salary scales: Senior Lecturer, £A.2,480 by £A.100 to £A.2,950; Lecturer, £A.1,660 by £A.100 to £A.2,360; with provision for superannuation on the F.S.S.U. basis. The initial salary will be fixed within the scale in relation to the successful candidate's qualifications and experience.

General conditions of appointment (including details of the provisions made for travelling expenses, housing, etc.) may be had from the Registrar of the University, or from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Other information may be had from the Professor. Applications close, in Australia and London, on June 30, 1961.

UNIVERSITY OF MELBOURNE

SENIOR DEMONSTRATOR OR DEMONSTRATOR IN BOTANY

Applications are invited for the above position. Applicants must have a minimum qualification of Bachelor of Science and at least two years' experience in research in Genetics or Cytology. The salary ranges are £A.1,400 to £A.1,600 for a senior demonstrator and £A.1,120 to £A.1,300 for a demonstrator. A single fare will be payable to an appointee from outside Victoria.

Applications, giving full details, should reach the Registrar, University of Melbourne, Parkville, N.2, Victoria, Australia, by May 31, 1961. An additional copy of application should be sent to the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1, to reach him by the same date. It is hoped to fill the vacancy as soon as possible.

F. H. JOHNSTON,
Registrar.

RESEARCH FELLOWSHIPS

R.R.E. Ministry of Aviation invites applications for Senior and Junior Research Fellowships tenable for three years at the Royal Radar Establishment, Malvern, commencing Autumn, 1961. There is a considerable choice of subjects within the fields of interest to the Establishment. These include experimental and theoretical research in low temperature physics, electrical and optical properties of semi-conductors, infra-red spectroscopy, micro-wave physics, electronics, radio-astronomy, shock waves, ionization phenomena in gases, physics of upper atmosphere. Candidates must be British subjects with normally first- or second-class honours degree in an appropriate subject, with evidence of a very high standard of ability in research. Exceptionally, a candidate without the requisite academic qualifications, but who can produce evidence of outstanding ability in research, may be admitted. At least two years' postgraduate experience required for Junior Research Fellowships (age preferably 23 to 26) and three years for Senior Research Fellowships (age preferably 26 to 30). Remuneration according to individual merit in ranges £1,325 to £1,640 (Senior Research Fellowship), £910 to £1,220 (Junior Research Fellowship) a year. Superannuation under F.S.S.U. At expiry of Fellowship the holder, if of suitable age, can be considered for an established (pensionable) post through a Civil Service Commission Open Competition.

Application forms and booklet from the Director, R.R.E., Malvern, Worcestershire, to whom they must be returned by April 24, 1961.

UNIVERSITY OF HONG KONG

READERSHIP IN MECHANICAL ENGINEERING

Applications are invited for the above-mentioned post. Applicants must be graduates of a British Commonwealth University or equivalent, and must be Corporate Members of the Institution of Mechanical Engineers, with teaching experience at university level. Preference will be given to those with special qualifications in Engineering Thermodynamics. Annual salary (superannuable) is £2,500 (man) or £1,900 (woman), together with an expatriation allowance of £300 a year if applicable. Salaries are under review. The equivalent of income tax in the Colony is comparatively low. First-class sea passages are provided for expatriate staff and their families on first appointment and leaves. Accommodation at reasonable rental is provided for those receiving expatriation allowance.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Hong Kong and London, on May 26, 1961.

SURREY EDUCATION COMMITTEE

EWELL COUNTY TECHNICAL COLLEGE, REIGATE ROAD, EWELL SCIENCE DEPARTMENT

Required September 1, 1961: (a) Lecturer, (b) Assistant Grade B. For graduates to teach applied biology; experience in microbiology will be specially considered; teaching and industrial experience an advantage. Salary scales: Lecturer, £1,370 by £35/£40 to £1,550; Grade B, £700 by £27 10s./£37 10s. to £1,150 plus London allowance £38 or £51 according to age and experience.

Addressed envelope to Principal for further details and application form to be returned by April 28.

UNIVERSITY OF WESTERN AUSTRALIA

FACULTY OF MEDICINE
LECTURESHIP IN BIOCHEMISTRY

Applications are invited for appointment to the above-named position in the Department of Biochemistry. The Department provides courses for undergraduate students in Faculties of Agriculture, Dental Science, Medicine and Science. Courses for postgraduate students in Science and for Ph.D. candidates are also offered. The salary range for the position is £A.1,750 by £A.75 to £A.2,350 per annum, with superannuation similar to F.S.S.U. The appointee will be required to commence duties as early as possible.

It is important that intending applicants obtain details of the procedure to be followed in applying for the post and a copy of the Conditions of Appointment, before submitting their applications. This information is available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Australia and London, on May 31, 1961.

"SHELL" RESEARCH LIMITED

TUNSTALL LABORATORY

(Sittingbourne, Kent)

DIVISION OF BIOCHEMISTRY

BIOCHEMIST

preferably with training and a degree in Biochemistry, and postgraduate and post-doctoral research experience is required to inaugurate and administer the Division of Biochemistry in this Laboratory. A medical qualification would be an advantage.

The duties of this post will consist of research into the biochemistry of toxicants and chemical pathology of intoxication. This is a senior position, and applicants will be remunerated accordingly.

Salary in accordance with age, qualifications and experience. Five-day week, staff restaurant, excellent pension scheme. Please write giving details of qualifications and experience to:

Personnel Recruitment/B.C.,
"Shell" Research Limited,
St. Helen's Court,
Great St. Helen's,
London, E.C.3.

UNICAM INSTRUMENTS LIMITED

PHYSICISTS

The research and development department of UNICAM INSTRUMENTS LTD. has a number of vacancies for graduate physicists with an interest in spectroscopic instruments in the ultraviolet, infrared and radio-frequency fields. A good honours degree is required, postgraduate research or engineering experience would be an advantage, and the ability to lead a small project team will be necessary. The salary offered will be appropriate to qualifications and experience.

Please reply to Unicam Instruments Ltd., Arbury Road, Cambridge, quoting reference E.D.34

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

Physicist, Engineer, or Biological Scientist with interest and experience in instrument development required to work with the Professor of Epidemiology on problems connected with the measurement of environmental and physiological variables in population groups. Appointment for two years in first instance. Successful applicant will be seconded to the Bio-Engineering Laboratory of the Division of Human Physiology, National Institute of Medical Research. Salary scale £800 to £1,000, depending on age and experience. Appointment to start June, 1961.

Applications to the Dean, London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.

UNIVERSITY OF WALES

A number of Fellowships, each of the annual value of £650 with the payment of approved fees and tenable for two years, will be awarded in 1961 to graduates of the University of Wales. Candidates for the Fellowships should send their applications to the Registrar, University Registry, Cathays Park, Cardiff, not later than June 1, 1961.

Further information may be obtained from the Registrar.

UNIVERSITY OF EDINBURGH

DEPARTMENT OF ELECTRICAL ENGINEERING

Applications are invited for the posts of Assistant and Lecturer in the new department of Electrical Engineering, to take up duties as soon as possible. Applicants should have a good honours degree in electrical engineering, with special interests and experience in one of the following branches: electrical machines, microwaves, plasmas, computer design techniques, solid-state electronics. New laboratories are being equipped and courses being planned which will give considerable individual responsibility to the Lecturers. Assistants would be expected to undertake research for a higher degree. Salary scales: Assistant, £800 by £50 to £950 per annum; Lecturer, £1,050 by £50 to £1,250; Bar: £1,300 by £50 to £1,400 by £75 to £1,850 per annum. Placement on the scales will be according to qualifications and experience. The posts are subject to superannuation, and family allowance is payable where applicable.

Further particulars may be obtained from the undersigned, with whom applications (six copies), giving the names of two referees, should be lodged not later than April 29, 1961.

CHARLES H. STEWART,
Secretary to the University.

SOUTH-WEST ESSEX TECHNICAL COLLEGE AND SCHOOL OF ART

FOREST ROAD, WALTHAMSTOW, E.17

Senior Lecturer in Applied Biochemistry required as soon as possible. The person appointed will be responsible for the teaching of Biochemistry and related subjects, paper chromatography, low and high voltage paper electrophoresis, and vapour phase chromatography, to H.N.C., B.Sc., and Grad.R.I.C. students and in the Laboratory Technician courses as well as in the special and post-graduate courses. Experience in the field of nucleic acid chemistry, enzyme chemistry, or radioactive tracer techniques, or interest in Electronic Instrumentation, is an added recommendation. Candidates should possess high academic qualifications, have teaching experience and provide evidence of research ability. Considerable research facilities are available and fundamental research will be encouraged. Salary within scale £1,550 to £1,750 per annum, plus £38 or £51 London allowance.

Apply by letter only (no forms) to the Clerk to the Governors, giving details of qualifications, training and experience, together with three recent testimonials or the names and addresses of three referees.

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

MANRESA ROAD, LONDON, S.W.3
DEPARTMENT OF GEOLOGY
RESEARCH ASSISTANTSHIPS

Applications are invited for two Research Assistantships in the Department (the appointments for which will be made in July). Candidates should possess a degree in Geology, with first- or second-class honours. The successful applicants will prepare as internal students for a higher degree under a Recognized Teacher of the University of London. The posts are tenable for two years but may be extended to three years. The salary will be £400 per annum. The assistants may be required to demonstrate for a maximum of six hours weekly for which an additional payment will be made.

Applicants should indicate the field of research or problem which they would like to investigate. In addition, they should give full particulars of their career and the names of two referees. Applications should be received not later than June 9 by the Clerk to the Governors.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

The Department of Electrical Engineering has vacancies for Lecturers in fields including: (i) electrical machines; (ii) electric traction; (iii) automatic control—mathematical aspects; (iv) electron physics—vacuum and plasma devices. The department is soon to occupy a new building with modern equipment, and research is in progress in all these fields. Candidates will, in general, be expected to participate in postgraduate teaching and research. Salaries in scale £1,050 by £50 to £1,400 by £75 to £1,550 (bar) by £75 to £1,850 per annum, plus £60 per annum London allowance, family allowances and F.S.S.U. membership. Appointments may be made in the higher part of this range in the case of suitably qualified candidates.

Apply to Head of Department of Electrical Engineering, Imperial College of Science and Technology, London, S.W.7.

GALLAHER LIMITED

CIGARETTE AND TOBACCO MANUFACTURERS

require the services of a

RESEARCH CHEMIST

in the

RESEARCH DEPARTMENT OF THEIR CENTRAL LABORATORY BELFAST

Candidates should possess an Honours Degree in Chemistry (or an equivalent qualification), with a special interest in Physical Chemistry. Some experience in Gas Chromatography and Ultra-violet Spectrophotometry, together with an interest in Statistical methods, would be an advantage. Candidates should preferably be within the age limit 23 to 30 years, although consideration will be given to a candidate above the upper limit. The Company operates on a five-day week, and their is a generous contributory Staff Pension Scheme. Salary will be commensurate with age and experience.

Applications should be forwarded to: Chief Chemist, Gallaher Limited, Virginia House, 138 York Street, Belfast, 15.

MANCHESTER COLLEGE OF SCIENCE AND TECHNOLOGY

(FACULTY OF TECHNOLOGY IN THE UNIVERSITY OF MANCHESTER)

Applications are invited for two Lectureships, an Assistant Lectureship and a Demonstratorship in the Department of Mathematics in the College, with corresponding title and status in the University of Manchester. Candidates should normally be graduates who are keenly interested in a branch of mathematics (especially analysis), statistics or applied mechanics, and who are prepared to undertake and, in the case of the more senior appointments, supervise research for higher degrees. Salary: Lecturer, £1,050 to £1,850 per annum, Assistant Lecturer, £800 to £950 per annum, Demonstrator, £675 to £700 per annum. F.S.S.U. and family allowances.

Application forms and further particulars may be obtained from the Registrar, The Manchester College of Science and Technology, Manchester, 1, to whom applications should be forwarded by Saturday, April 22, 1961.

SIR JOHN CASS COLLEGE

JEWRY STREET, LONDON, E.C.3

RESEARCH ASSISTANTS

The Governors of Sir John Cass's Foundation intend to appoint Research Assistants in the Departments of Botany and Zoology, Chemistry, Mathematics, Metallurgy (Geology) and Physics, and invite applications from graduates in these subjects who wish to become qualified by research, for a Higher Degree. The College is recognized by the University of London, and Research Assistants are registered as Internal students for the M.Sc. or Ph.D. degrees of the University. Appointments will be made for one year in the first instance, renewable, subject to satisfactory progress, for two further years. The commencing date is September 1, 1961, and the basic stipend is £400 a year, to which may be added a further sum of about £200 a year for an assistant who acts as demonstrator for six hours weekly during College terms.

Further particulars and forms of application may be obtained from the Secretary of the College.

UNIVERSITY OF EXETER

Applications for the post of Research Assistant, for work on volatile inorganic compounds in collaboration with Dr. L. H. Long, are invited from chemists preferably with two or three years research experience. Salary £850 per annum, plus F.S.S.U. benefits.

Applications (eight copies), giving a brief account of career and nominating two referees, should reach the Secretary of the University by May 8.

GEOLOGICAL SURVEY AND MUSEUM (D.S.I.R.), London, S.W.7, requires Geophysicists as Experimental Officers and Assistant Experimental Officers. Duties mainly concern outdoor geophysical surveys anywhere in the United Kingdom. Qualifications: (Experimental Officer) Pass degree or equivalent in geology with ancillary physics or mathematics, or in physics or mathematics with ancillary geology. (Assistant Experimental Officer) G.C.E. "A" level in geology, mathematics or physics, and in another science subject. Over 22, pass degree expected. Salary ranges: Experimental Officer, £1,147 to £1,396; Assistant Experimental Officer, £503 (age 18) to £856 (age 26) to £1,038.—Forms from Ministry of Labour, Technical and Scientific Register (K), 26 King Street, London, S.W.1, quoting G.98/1A.

UNIVERSITY OF HONG KONG

LECTURESHIPS IN CHEMISTRY

Applications are invited for two Lectureships in Chemistry, one in Physical Chemistry and the other in Inorganic Chemistry. A suitably qualified applicant may be appointed as Senior Lecturer. The present salary scales, which are under review, are (including the allowance payable to expatriate staff): Senior Lecturer (man), £2,250 by £75 to £2,550, (woman) £1,750 by £60 to £1,990; Lecturer (man), £1,800 by £50 to £2,400, (woman) £1,425 by £40 to £1,905. The equivalent of income tax in the Colony is comparatively low. First-class sea passages are provided for expatriate staff and their families on first appointment and leaves. Accommodation at reasonable rental is provided for those receiving expatriation allowance.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1. Applications close, in Hong Kong and London, on May 31, 1961.

RESEARCH CHEMISTS

MEDICAL RESEARCH COUNCIL GRANT AND PHYSICAL CHEMIST

Applications are invited for two posts at the British Gelatine and Glue Research Association, 2a Dalmeny Avenue, London, N.7.

1. Graduate for fundamental research on the structure and metabolism of collagen under the direction of Dr. A. Courts, in collaboration with the M.R.C.'s Rheumatism Research Unit. (Grant from the Medical Research Council.)
2. Physical Chemist, preferably with several years of postgraduate experience, for fundamental studies on gelation.

Salaries will be in accordance with qualifications and experience. It is possible that, in Post 1, the holder will have the opportunity to obtain a higher degree.

Applications to the Director of Research by May 23, 1961.

THE INTERNATIONAL NICKEL COMPANY (MOND) LIMITED

requires a

DEVELOPMENT OFFICER

for work in connection with Chemical Products, involving the promotion of new chemical applications of nickel in fields of catalysis, co-ordination chemistry, and agriculture. Candidates, under 40 years of age, should have a sound scientific and technical training, preferably with some years practical experience in an appropriate branch of the chemical industry.

Pension and assurance schemes are in operation and, in appropriate cases, assistance can be given with housing.

Apply, giving full particulars of qualifications, experience, age, salary required, etc., to The Manager, General Division, Development and Research Department, The International Nickel Company (Mond) Limited, Thames House, Millbank, London, S.W.1. Mark envelope "Confidential D.34N."

UNIVERSITY OF MANCHESTER

Applications are invited for the post of Lecturer in Cytology in the Departments of Botany and Zoology in the Faculty of Science. Candidates should have a wide interest in the subject so as to be able to lecture to students of both departments. Duties to commence on October 1, 1961. Membership of F.S.S.U. and Children's Allowance Scheme. Salary on a scale £900 to £1,650 per annum, initial salary according to qualifications and experience.

Applications should be sent not later than April 25, 1961, to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

UNIVERSITY OF LIVERPOOL

Applications are invited for Research Fellowships in Experimental Physics. Candidates should be of Ph.D. standard, with special aptitude for research in high or low energy nuclear physics. The Fellowships are tenable for not more than three years, at an initial emolument within the range £600 to £800 per annum, with F.S.S.U. benefits.

Applications, three copies, stating age, details of qualifications and experience, publications, research work in progress and completed, together with the names of two referees, should be received not later than May 1, 1961, by the Registrar, from whom further particulars may be obtained. (Candidates overseas who find it more convenient to do so may send one copy only by airmail). Quoting reference CV/N.

THE POLYTECHNIC

309 REGENT STREET, W.1

DEPARTMENT OF MATHEMATICS AND PHYSICS

Applications are invited for the full-time post of Grade B Lecturer in Physics, duties to commence on September 1, 1961. Candidates should possess a good honours degree in physics and be able to lecture on the subject up to a degree standard. Applications from physics students expecting to graduate in the summer of 1961 will be considered. Research work is encouraged in the Department. The salary scale for a Graduate Grade B Lecturer commences at £790 per annum rising by annual increments of £27 10s. to £1,240 plus London allowance of £38 or £51 per annum. Additional allowances are payable in respect of a good honours degree and training.

A form of application, which should be returned not later than April 28, 1961, may be obtained by sending a stamped addressed foolscap envelope to the undersigned.

J. E. RICHARDSON,
Director of Education.

UNIVERSITY OF BRISTOL

Applications are invited for the post of Junior Fellow in Pharmacology. Medical qualification desirable but not essential. Initial salary £800 to £950 per annum, according to qualifications and experience, together with superannuation and children's allowances. The successful candidate will be expected to devote much of his time to research. The post would be suitable for a candidate who wishes to read for a Higher Degree.

Further particulars may be obtained from the undersigned, to whom applications (six copies), with the names of three referees, should be sent not later than May 15, 1961.

H. C. BUTTERFIELD,
Registrar and Secretary.

U.S.A.

UNIVERSITY OF ALABAMA MEDICAL SCHOOL

GENERAL BIOCHEMIST

Biochemist required for Gastroenterology Research Laboratories with special interest in gastric secretion (electrolytes, pepsin), small bowel absorption and lipid analysis. Research experience essential. Starting salary according to experience, but would not be less than $7,000 per annum.

MEDICAL TECHNICIAN

Medical Technician required for Gastroenterology Research Laboratories with special interest in gastric secretion (electrolytes, pepsin), small bowel absorption and lipid analysis. Research experience desirable but not essential.

Applications should be addressed to:
Basil I. Hirschowitz, M.D.,
Director, Division of Gastroenterology,
University of Alabama Medical Center,
Birmingham, Alabama.

UNIVERSITY OF EDINBURGH

DEPARTMENT OF PHYSIOLOGY

Applications are invited for the post of Lecturer in the Department of Physiology. Salary scale: £1,050 by £100 to £1,450; Bar: £1,600 by £100 to £1,900 per annum, with placement according to qualifications and experience, and with superannuation benefit and family allowance where applicable. Some experience of research on the cardiovascular system in man or animals an advantage. Candidates should have an honours degree in physiology or an allied subject, or equivalent training. The successful candidate will be expected to take up duty on October 1, 1961.

Further particulars may be obtained from the undersigned, with whom applications (six copies), giving the names of two referees should be lodged not later than May 1, 1961.

CHARLES H. STEWART,
Secretary to the University.

UNIVERSITY OF CANTERBURY
CHRISTCHURCH, NEW ZEALAND
CHAIR OF GEOGRAPHY

Applications are invited for the above-mentioned Chair, this vacancy being due to the appointment of Professor L. L. Pownall as Vice-Chancellor and Rector of the University of Canterbury. The Chair will become vacant on May 1, 1961, but the University will be prepared to arrange with the successful applicant a convenient date on which he should take up his duties. The salary attached to the Chair is at the rate of £2,800 per annum.

Further particulars are available from the Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1, or from the Registrar, University of Canterbury, Christchurch, New Zealand. Applications close, in New Zealand and London, on May 31, 1961.

UNIVERSITY OF SHEFFIELD
COUNTY LABORATORIES RESEARCH FELLOWSHIP

Applications are invited for:

A Research Fellowship to work on hair growth in collaboration with Dr. F. J. Ebling in the Department of Zoology. The value of the fellowship in the first year will be up to £1,050 plus F.S.S.U., and it will be renewable annually. Applicants should have training in zoology, physiology or biochemistry, and some research experience; a Ph.D. would be an advantage. Further particulars can be obtained from Dr. Ebling.

A Graduate Research Assistant to work on hair growth. Applicants should have training in zoology, physiology or biochemistry. Salary £750 plus F.S.S.U.

Applications for both posts, with the names of two referees, should be sent to Dr. F. J. Ebling.

UNIVERSITY OF LIVERPOOL

Applications are invited for two posts of Lecturer in the Department of Electrical Engineering. The initial salary will be within the range £1,050 to £1,250 per annum, according to age, qualifications and experience. Research interest and experience in one or more of the following subjects would be an advantage, but is not essential: electronic circuit techniques, electrical discharges in gases, high voltage engineering, plasma engineering.

Applications, stating age, academic qualifications and experience, together with the names of three referees, should be received not later than May 1, 1961, by the Registrar, from whom further particulars of the conditions of appointment may be obtained. Quoting Reference CV/N.

UNIVERSITY OF EDINBURGH
DEPARTMENT OF AGRICULTURE

Applications are invited for the post of Lecturer in the Department of Agriculture. Candidates should have a special interest in crop husbandry. Salary scale: £1,050 by £50 to £1,250; bar: £1,300 by £50 to £1,400 by £75 to £1,850 per annum, with placement according to qualifications and experience, and with superannuation benefit and family allowance where applicable. The successful candidate will be expected to take up duty on October 1, 1961.

Further particulars may be obtained from the undersigned, with whom applications (six copies), giving the names of two referees, should be lodged not later than April 29, 1961.

CHARLES H. STEWART,
Secretary to the University.

UNIVERSITY OF SHEFFIELD
POST-DOCTORAL FELLOWSHIP

Applications are invited for a Post-doctoral Fellowship (stipend £1,050 per annum or £950 plus F.S.S.U.) in the Department of Chemistry. The Fellow will be expected to carry out researches into the reactions of halogen atoms with organic molecules in collaboration with Dr. J. M. Tedder.

Applications, together with the names and addresses of three referees, should be sent to the Registrar, The University, Sheffield 10, by May 6, 1961.

HAREFIELD AND NORTHWOOD GROUP
HOSPITAL MANAGEMENT COMMITTEE

Chief Laboratory Technician I required at Harefield Hospital. 610 Chest and General Beds. Salary £905 by £30 (6) to £1,085 per annum, plus London weighting.

Applications, quoting two referees to Group Secretary, Mount Vernon Hospital, Northwood, Middlesex, by April 27, 1961.

THE ROYAL COLLEGE OF SCIENCE AND TECHNOLOGY, GLASGOW

IMPERIAL CHEMICAL INDUSTRIES RESEARCH FELLOWSHIPS

Applications are invited for Imperial Chemical Industries Research Fellowships tenable at this College from October 1, 1961.

Fellowships may be awarded for the purpose of carrying out original research in:

APPLIED MATHEMATICS,
CHEMISTRY,
ENGINEERING,
METALLURGY,
MICROBIOLOGY, and
PHYSICS,

for a period not exceeding three years. Applicants should preferably hold the degree of Ph.D., or equivalent research experience. Annual stipend will depend on age, qualifications and experience, but will be within the range £800 to £1,100 together with F.S.S.U. benefits.

Applications (two copies) stating details of career, qualifications and research interests, together with the names of two referees, should reach the **Secretary of the College, George Street, C.1,** from whom further inquiries may be made not later than May 15, 1961.

CHEMIST

A leading food manufacturing Company wish to appoint a Chemist to the staff of their new Product Development Group.

The Chemist appointed will be concerned with the development of canned products. Candidates aged not over 35 years, must have full knowledge of canning technology. The Company's premises are situated in the West London area.

Applicants are asked to write giving full details of age, education, qualifications and experience to Box No. G8808, c/o Whites, 72 Fleet Street, London, E.C.4.

McGILL UNIVERSITY
Montreal, Canada

TECHNICIAN
IN DEPARTMENT OF PHYSIOLOGY

required to work in an Aviation Medical Research Unit. Experience in electrophysiological technique an advantage. Salary range $3,000 to $4,500 according to experience. Apply giving details of previous experience Dr. Melvill Jones, Institute of Aviation Medicine, Farnborough, Hants.

UNIVERSITY OF BRISTOL

Applications are invited for the post of Assistant Lecturer (Grade III) in Chemical Physiology (Veterinary). Initial salary in the range £800 to £950 per annum, according to qualifications and experience, together with superannuation and children's allowances.

Applications (six copies), with the names of three referees, should be forwarded so as to reach the undersigned, from whom further particulars may be obtained, not later than May 17, 1961.

H. C. BUTTERFIELD,
Registrar and Secretary.

OLDCHURCH HOSPITAL ROMFORD, ESSEX
(709 Beds)
RADIOTHERAPY DEPARTMENT

Senior Technician or Technician required for the above Department. Duties include Physics Workshop, Isotope Laboratory, Radium and Mould Room work. Instrument or Physics Workshop experience essential. Salary £570 to £710 per annum; senior grade, £710 to £905 per annum would be applicable to suitably qualified person.

Applications, quoting Ref. 17/39, giving full details, including age and experience, together with names of two referees and/or copy of testimonials to the Group Secretary, Romford H.M.C., Oldchurch Road, Romford.

AUSTRALIA
THE UNIVERSITY OF NEW SOUTH WALES
SCHOOL OF MATHEMATICS

The School of Mathematics at the University of New South Wales wishes to appoint two Senior Lecturers and two Lecturers. One Senior Lecturer will be appointed to the Broken Hill Division of the University.

The School prepares students in the Faculties of Arts and Science for pass and higher degrees in pure or applied Mathematics, or mathematical statistics. In addition, students of engineering and applied science receive mathematical training linked with their own special interests. As there are a considerable number of part-time students, some evening lecturing is inevitable, but this is kept to a minimum. The School is composed of the Departments of Pure Mathematics, Applied Mathematics, Mathematical Statistics, and Engineering and General Mathematics, and Lecturers work mainly in their chosen department. They may, however, be required to assist with elementary courses in any subject. There are good facilities for specialized research and postgraduate teaching. The School has a finely equipped Computing Laboratory which is available to research workers throughout the University. The staffs of the Schools of Mathematics and Electrical Engineering work together on research projects, using a large electronic digital computer (UTECOM, an English Electric Deuce machine).

Mathematicians who are interested in the positions offered by the School should have the following qualifications: Senior Lecturer: A higher degree or equivalent qualifications. Lecturer: A degree with honours or equivalent qualifications. Experience or research interests in the theory of statistics, or in topology, set theory, or integral transform theory in pure mathematics would be particularly valuable.

Salary: Senior Lecturer, £A.2,586 range £A.3,036 per annum. Lecturer, £A.1,766 range £A.2,471 per annum. Commencing salary will be determined by qualifications and experience. First-class ship fares to Sydney of appointees and their families will be paid. Subject to passing a medical examination appointees will be eligible to contribute to the State Superannuation Fund.

Four copies of applications, including the names of two referees, should be lodged with the Agent-General for New South Wales, 56 Strand, London, W.C.2, and a copy forwarded to the Appointments Section, University of New South Wales, Box 1, Post Office, Kensington, N.S.W., Australia, by airmail before June 9, 1961. Applicants outside the United Kingdom and Eire need only submit one copy of their application to the London address in addition to that sent to Sydney.

QUEEN'S UNIVERSITY
KINGSTON, ONTARIO, CANADA
LECTURER IN CHEMISTRY

Applications are invited for the above post. Candidates should have research experience. The appointee will be expected to teach undergraduates and carry on fundamental research. The appointment is probationary for the first two years.

Applications should include names of two referees to whom application may be made for references. Details of papers published and research interests should also be given. Further particulars can be obtained from Professor J. K. N. Jones.

ROYAL VETERINARY COLLEGE
(UNIVERSITY OF LONDON)

Applications are invited for a Lectureship in Animal Nutrition in the Department of Animal Husbandry and Veterinary Hygiene, tenable at the College's field station near Potters Bar, Middlesex. Facilities for research will be available. Postgraduate experience in biochemistry would be an advantage. Salary scale £1,050 by £50 to £1,400 by £75 to £1,550; then, subject to review, by £75 to £1,850. London allowance £60 per annum payable in addition. F.S.S.U. and children's allowances. Commencing salary within the scale according to experience and qualifications.—Application forms, obtainable from the Secretary, Royal Veterinary College, Royal College Street, London, N.W.1, should be returned not later than May 15, 1961.

UNIVERSITY COLLEGE OF SWANSEA

Applications are invited from suitably qualified candidates for an Assistant Lectureship or Lectureship in Pure Mathematics. Salary scales: Lectureships, £1,050 to £1,850 per annum; Assistant Lectureships, £800 to £950 per annum. F.S.S.U. benefits and family allowances.

Further particulars can be obtained from the Registrar, University College, Singleton Park, Swansea, by whom applications (six copies) must be received not later than Saturday, April 29, 1961.

UNIVERSITY OF MANCHESTER

Applications are invited for two posts at the grade of Assistant Lecturer in the Department of Mathematics. For one of the posts qualifications are required in the field of pure mathematics and for the other in applied mathematics. Salary on a scale £800 to £950 per annum, with membership of the F.S.S.U. and children's allowance scheme.

Applications should be sent not later than April 27, 1961, to the Registrar, the University, Manchester, 13, from whom further particulars and forms of application may be obtained.

ZOOLOGICAL SOCIETY OF LONDON
RESEARCH FELLOWSHIPS AND STUDENTSHIPS IN ANIMAL REPRODUCTION

The Council of the Zoological Society of London invites further applications for Research Fellowships and Studentships in animal reproduction which have been endowed by a grant from the Ford Foundation. Those who are appointed will be expected to contribute to the scientific understanding of reproductive mechanisms, but their choice of subject within this broad field will not be restricted. They will be provided with newly built and equipped laboratories at Regent's Park, but, in addition, it is intended that they should be associated with the laboratory of an appropriate leading authority in their chosen field of study. There will be ample provision for research expenses and technical services, and special facilities for the study of the Society's collections at Regent's Park and at Whipsnade will be provided.

Two types of appointment are contemplated.

(1) Research Studentships. These are intended for recent graduates who wish to study the biology of reproduction, and to receive research training which would lead to a Ph.D. degree. Salaries will range from £450 to £650 for up to three years. Applicants should provide the names of two referees and a statement of the branch of the subject in which they are interested.

(2) Research Fellowships. These are intended to be post-doctoral Fellowships and applicants should already be experienced and capable of independent research. The appointments will be for periods of one to five years, and salaries will range from £800 to £1,850 according to experience, plus F.S.S.U. benefits. Applicants should provide the names of two referees and proposals for the programme of research which they wish to undertake, together with an estimate of the costs involved.

Applicants should write as soon as possible to the Honorary Secretary of the Zoological Society of London, Regent's Park, London, N.W.1. The latest date for consideration of applications is May 15, 1961.

DEPUTY CHIEF ANALYST. QUALIFIED chemists are invited to apply for this appointment in new City of London Research Laboratories. The work is varied but mainly concerned with food products. Experience in a Public Analyst Laboratory an advantage.—Write, stating age, qualifications and experience, to Box 961, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

UNIVERSITY OF MANCHESTER
SYBIL MARY PILKINGTON FELLOWSHIP FOR RESEARCH INTO DISEASES OF THE BLOOD

Applications are invited for the Sybil Mary Pilkington Fellowship for research into Diseases of the Blood, with particular reference to the causation, treatment and cure of leukaemia in man; the research would normally be carried out in the Department of Haematology of the University in Manchester Royal Infirmary. The Fellowship is open to persons who have obtained a medical qualification registrable in the United Kingdom, the Dominions or any other country. The stipend, which is according to qualifications and experience will be within the range of £1,000 to £1,500 per annum, and the Fellowship is tenable for one year in the first instance. The Fellowship is now vacant for 1961, and the appointed Fellow would be expected to take up the Fellowship on a date to be arranged.

Applications must be sent not later than May 8, 1961, to the Registrar, the University, Manchester 13, from whom further particulars and forms of application may be obtained.

PHARMACOLOGIST

required to work in London for the first two years in an academic department and thereafter in a newly created Research Laboratory in London.

Non-contributory Pension and Life Assurance Scheme and excellent salary; scope for promotion.

Write, giving full details of age, qualifications, experience and salary required, to the Managing Director, Biorex Laboratories Limited, 47–51 Exmouth Market, London, E.C.1.

BRITISH COUNCIL
IRAN
TEHERAN UNIVERSITY

Applications are invited for the post of Professor of Zoology in Teheran University. Duties, to direct the Department and organize teaching and research. Candidates should have British university qualifications, with relevant teaching experience. Salary on scale equivalent to £1,698 to £2,830 a year. Furnished accommodation for single men; housing allowance, equivalent to £566 a year for married men. Superannuation may be maintained. Contracts with Teheran University and British Council, for one year, renewable. Fares paid, and for family. Secondment may be arranged.

Write, quoting N.5/30161 and enclosing stamped, addressed foolscap envelope, to Director, Recruitment Department, British Council, 65 Davies Street, London, W.1, for further particulars and application form to be returned within two weeks of receipt.

UNIVERSITY COLLEGE OF THE WEST INDIES

Applications are invited for Lectureship in Inorganic Chemistry. Duties to be assumed by October 1, 1961, or as soon as possible thereafter. Salary scale: £1,050 by £50 to £1,400 by £75 to £1,850 per annum, plus local allowance of £250 per annum (pensionable). Entry point determined by qualifications and experience. Child allowance. F.S.S.U. Unfurnished accommodation at rental of 10 per cent of basic salary. Up to five full passages on appointment, termination, and on triennial study leave.

Detailed applications (six copies), naming three referees, by May 10, 1961, to Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1, from whom further particulars may be obtained.

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING
(UNIVERSITY OF READING)
BIOMETRICIAN

Graduate with mathematical and biological interests required in the Section of Statistics. Duties involve consultation and research on design and analysis of experiments for which a knowledge of statistics is desirable, though not initially essential as training will be given. Appointment in Scientific Officer (£717 to £1,222) or Senior Scientific Officer (£1,302 to £1,654) grade, according to age and experience.

Applications, naming two referees, to Secretary, N.I.R.D., Shinfield, Reading. Quote ref. 61/12.

LUTON COMMITTEE FOR EDUCATION
LUTON COLLEGE OF TECHNOLOGY

Vacancies for September due to increase in College Establishment for:—

DEPARTMENT OF SCIENCE

(a) Lecturer in Botany. Good Honours Degree and ability to teach to London B.Sc. (External) standard necessary.

(b) Grade "B" Assistant in Physics. Good degree or equivalent required; ability to teach to London B.Sc. (External) standard and to engineering students taking Ordinary and Higher National Diploma.

Salary scales: Lecturer, £1,370 by £15 to £1,550; Grade "B" Assistant, £700 by £27 10s. to £1,150.

Send s.a.e. (foolscap) for application form and further details to Borough Education Officer, 63-69 Guildford Street, Luton.

HAREFIELD HOSPITAL
HAREFIELD, MIDDLESEX

Biochemist (Basic Grade) required. 610-bed Chest and General Hospital. London weighting payable.

Applications, quoting two referees, to reach Hospital Secretary by April 28, 1961.

CHEMICAL TECHNICIAN REQUIRED FOR research. Advanced level chemistry and biology minimum requirements. Whitley Council rates of pay according to qualifications and experience.—Applications, with names of two referees, to Dr. B. E. Clayton, Department of Chemical Pathology, the Hospital for Sick Children, Great Ormond Street, W.C.1.

PHYSICAL CHEMIST REQUIRED FOR investigations on the structure and properties of products bonded by hydrated calcium silicates. Research experience in X-ray powder diffraction methods and some knowledge of phase equilibria studies desirable. Applicants should have at least second-class honours degree. The post, which is permanent, with superannuation under the F.S.S.U. scheme, will be graded and the salary commensurate with the qualifications and experience of the applicant selected. The laboratory and environment in Hertfordshire are pleasant, with good research facilities.—Apply, giving particulars of experience, etc., to Director of Research, Chalk Lime and Allied Industries Research Association, Church Street, Welwyn, Herts.

PRIVATE SECRETARY TO PROFESSOR, preferably with some knowledge of biology and/or anthropology, to work in Knightsbridge area. Age over 25. Salary up to £14 per week according to experience.—Write Box 963, T. G. Scott and Son, Ltd., 1 Clement's Inn, London, W.C.2.

BIOCHEMIST, NON-MEDICAL, BASIC grade, required for the Group Laboratory, Guildford. Qualifications, salary, etc., as defined by the Whitley Council.—Applications, giving full particulars and names of two referees, to the Hospital Secretary, St. Luke's Hospital, Guildford.

BIOCHEMISTS OR CHEMISTS (TWO) REquired to assist in research on: (a) Column chromatography of proteins and (b) Blood lipids in relation to coagulation. Appointment for one year in the first instance. Possibility of work for higher degree.—Applications as soon as possible to Professor of Chemical Pathology, Westminster Medical School, London, S.W.1.

SHREWSBURY SCHOOL. REQUIRED FOR September, 1961, Master to teach Physics. A highly qualified man could expect a substantial proportion of the "S" level work.—Apply immediately to the Headmaster, The Schools, Shrewsbury.

TRADE ANNOUNCEMENTS

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LECTURES AND COURSES

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Applications are invited for the following courses which will commence in September, 1961:

Graduateship of the Royal Institute of Chemistry, Part II. A three-term full-time course for those who, at the time of enrolment, have passed Part I, or who have been granted exemption from and have reached the standard of Part I.

Higher National Diploma in Chemistry. A two-year full-time course for the Higher National Diploma in Chemistry with special reference to Analytical Chemistry, open to those who have (a) A-level Chemistry with Physics and Mathematics taken beyond O level, or (b) O.N.C. Chemistry.

Further details and forms of application from Head of Department of Chemistry, Biology and Geology, Kingston Technical College, Fassett Road, Kingston-upon-Thames, Surrey.

BIRKBECK COLLEGE
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Part-time (evening) courses provided for Internal degrees in the Faculties of Arts and Science. Facilities also provided for full-time and part-time students reading for

(i) Higher Degrees in Arts and Science.
(ii) M.Sc., Crystallography by examination.
(iii) Academic Postgraduate Diplomas in Psychology, Numerical Analysis and Statistics.

The Department of Scientific and Industrial Research has accepted the Postgraduate Diploma Courses in Psychology and Numerical Analysis, and the M.Sc. Crystallography course, as suitable for tenure of its Advanced Course Studentships. Students intending to read for Higher Degrees in Science by thesis are invited to inquire of the College whether it has available any D.S.I.R. Research Studentships.

Applications for admission to the College should be made before June 1. Pamphlet and form of application may be obtained from the Registrar, Birkbeck College, Malet Street, W.C.1.

GRANTS & SCHOLARSHIPS

BRITISH OXYGEN FELLOWSHIPS

Applications are invited from British subjects who have graduated, or will graduate in 1961, for three Fellowships for research training. The value of these Fellowships lies between £350 and £700 per annum for two years, with a possibility of renewal for a third year, and grants may also be made to the University or College concerned towards the cost of equipment connected with the research which is undertaken.

The Fellowships will be awarded to enable research training to be obtained in any of the following fields: (a) Production of low temperatures. (b) Phenomena occurring at low temperatures. (c) Measurement of the properties of oxygen, nitrogen and other atmospheric gases. (d) High temperature production and utilization. (e) Use of Oxygen, Nitrogen or Argon in Metallurgy. (f) Metallurgical or electrical aspects of welding. (g) Use of Oxygen in Medicine.

Further particulars and application form may be obtained from the Secretary, British Oxygen Fellowships Committee, The British Oxygen Company Limited, Deer Park Road, London, S.W.19. Applications must be received by June 7, 1961.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Applications are invited for a Research Scholarship in Analytical Chemistry available from October 1, 1961, for two years in first instance in range £400 to £600 per annum (plus fees), depending upon general analytical experience. Award made by Mining & Chemical Products Ltd. for work on Controlled Potential Electrolysis leading to Ph.D.

Further particulars obtainable from Mr. L. S. Theobald, Reader in Analytical Chemistry, Chemistry Department, Imperial College, London, S.W.7.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

ESSO STUDENTSHIP IN CHEMICAL ENGINEERING

Applications are invited from men who hold, or expect to hold, an honours degree in one of the Physical Sciences or Engineering, for the Esso Studentship, founded by the Esso Petroleum Company Limited, tenable in the Department of Chemical Engineering at the above College from October, 1961. The value of the Studentship is £400 a year plus College fees.

Applications should be submitted to the Registrar, Imperial College, London, S.W.7, by April 29th, giving full particulars of previous industrial experience (if any), national service, and academic qualifications. The names of two referees should also be given.

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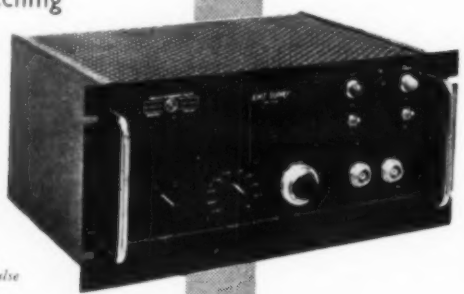

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Incidental Information

No. 14

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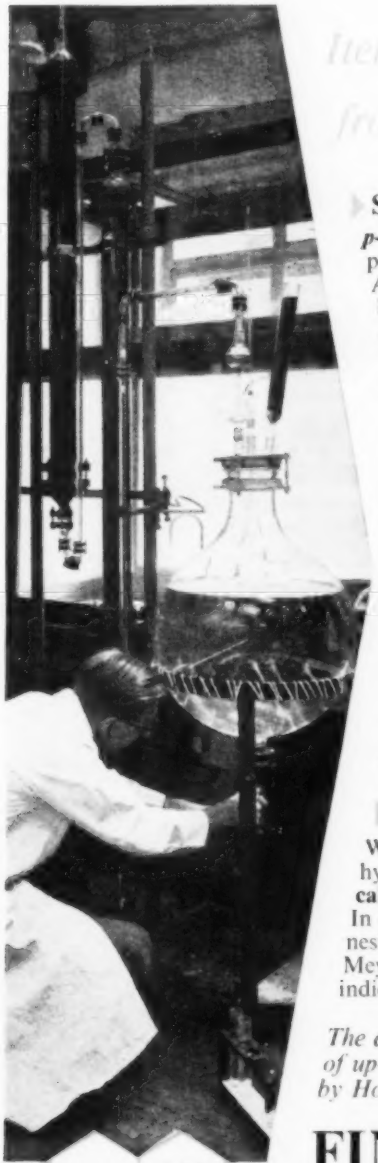

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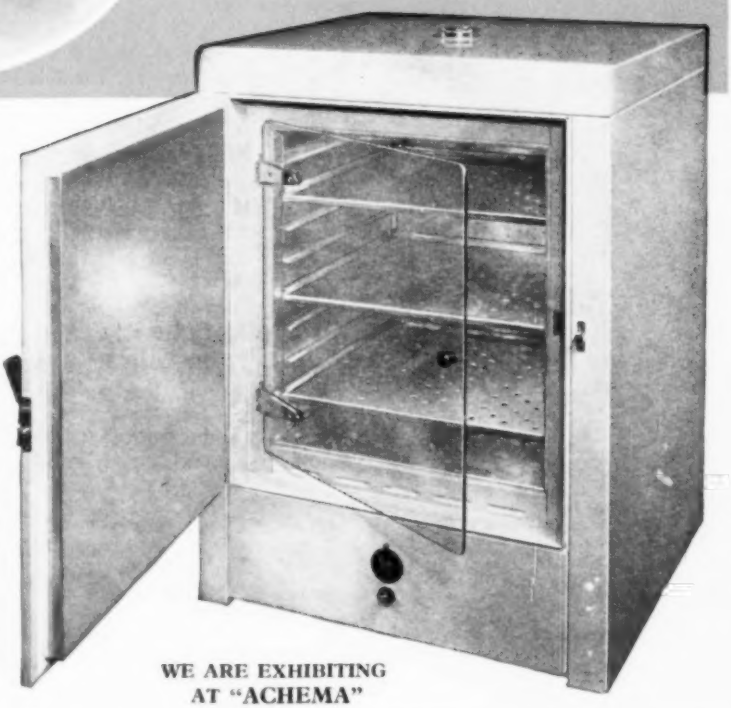

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